PRVD2008-03

Proposed Re-evaluation Decision

Thifensulfuron methyl

(publié aussi en français)

30 January 2008

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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ISBN: 978-0-662-47653-5 (978-0-662-47654-2)
Catalogue number: H113-27/2008-3E (H113-27/2008-3E-PDF)

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OVERVIEW

Proposed Decision for Thifensulfuron methyl

After a re-evaluation of the herbicide thifensulfuron methyl, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing thifensulfuron methyl in Canada.

An evaluation of available scientific information found that products containing thifensulfuron methyl have value in the food and crop industry and do not present unacceptable risks to human health or the environment. As a condition of the continued registration of thifensulfuron methyl use on various food, feed, industrial oilseed and fibre crops including wheat, barley, oats, flax, soybean, field tomato, forage grasses, imazethapyr-tolerant canola, and sulfonylurea-tolerant soybean, new risk reduction measures are proposed for the labels of all products. No additional data are being requested at this time.

The PMRA's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure. Re-evaluation draws on data from registrants, published scientific reports, information from other regulatory agencies and any other relevant information available.

This proposal affects all end-use products containing thifensulfuron methyl registered in Canada. Once the final re-evaluation decision is made, registrants will be instructed on how to address the new risk-reduction measures.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for thifensulfuron methyl and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessment of thifensulfuron methyl.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*

Proposed Re-evaluation Decision for Thifensulfuron Methyl

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What Does Health Canada Consider When Making a Re-evaluation Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration[2]. The Act also requires that products have value[3] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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2 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*

3 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies rigorous, modern hazard and risk assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in both humans (e.g. children) and organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

Before making a re-evaluation decision on thifensulfuron methyl, the PMRA will consider all comments received from the public in response to this consultation document[4]. The PMRA will then publish a Re-evaluation Decision document[5] on thifensulfuron methyl, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Is Thifensulfuron Methyl?

Thifensulfuron methyl is a selective systemic sulfonylurea herbicide. It is registered for postemergent use on various food, feed, industrial oilseed and fibre crops including wheat (spring, winter, and durum), barley, flax (CDC Triffid), oats (Prairie provinces and Peace River region of BC), soybean, field tomato, forage grasses (seedling or established), imazethapyr tolerant canola (Prairie provinces and Peace River region of BC), and sulfonylurea tolerant soybean (Eastern Canada only). Thifensulfuron methyl may be used alone or in co-formulation with tribenuron methyl or chlorimuron ethyl to control a wide spectrum of broadleaf weeds. Application is made once per year at a rate of 3.3–15 g a.i./ha by ground equipment only.

Health Considerations

Can Approved Uses of Thifensulfuron Methyl Affect Human Health?

Thifensulfuron methyl is unlikely to affect your health when used according to the revised label directions.

People could be exposed to thifensulfuron methyl by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the dose levels where no health effects occur and the dose levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing

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4 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*

5 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*

mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when using thifensulfuron methyl products according to label directions.

An acute over-exposure to thifensulfuron methyl can produce a variety of symptoms in animals and humans. Symptoms may include weight loss, diarrhea, yellow-stained perineal area and nasal discharge. Contact with the eye may cause slight corneal opacity and chemosis, mild conjunctivitis, and moderate iritis. Contact with the skin may cause slight erythema and edema.

Additional toxic effects include reduced serum sodium and increased relative organ weights. Effects noted at high doses in fetal rats include an increased incidence of absent renal papillae and small renal papillae. However, these effects are not likely to occur when thifensulfuron methyl products are used according to label directions. Based on the weight of evidence, thifensulfuron methyl is considered non-carcinogenic. A cancer risk assessment was not required.

Although there are no risks of concern based on current uses of thifensulfuron methyl, some additional protective measures have been proposed for inclusion on product labels, to update the label according to current standards (see Appendix XI).

Residues in Water and Food

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Human exposure to thifensulfuron methyl, including that of the most highly exposed sub population (e.g. children 1 to 6 years old), was estimated from residues in treated food commodities. This dietary exposure represents less than 0.1% of the acute reference dose and less than 5% of the chronic reference dose. Based on the Tier I computer modelling drinking water estimated concentrations (DWECs), exposure that may occur from drinking water is not of concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for the *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

MRLs for thifensulfuron methyl are currently specified for flax, canola and tomatoes or processed foods derived from these foods. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. The proposed amendments to the default MRL for thifensulfuron methyl can be found in the Science Evaluation Section 8.1.2 of this consultation document.

Risks in Residential and Other Non-Occupational Environments

Residential and other non-occupational risks are not of concern.

Thifensulfuron methyl is not registered for use in any residential areas; therefore, no residential or other non-occupational risks are expected.

Occupational Risks From Handling Thifensulfuron Methyl

Occupational risks are not of concern.

Based on both the precautions and directions for use on the original product labels reviewed for this re-evaluation, and also considering the use of appropriate protective equipment, the risk estimates associated with mixing, loading and applying activities meet current standards for all use scenarios and are not of concern. The proposed personal protective equipment are long pants, long-sleeved shirt, socks, chemical-resistant gloves and footwear.

Postapplication risks are not of concern.

Occupational postapplication risk assessments consider exposures to workers re-entering treated sites. Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation, and considering proposed protective measures (i.e. personal protective equipment, revised re-entry interval), the postapplication exposure risk estimate for re-entry workers performing high exposure activities (irrigation, scouting, thinning, hand pruning, hand weeding, staking, training, tying and hand harvesting) meet current standards and are not of concern.

Environmental Considerations

What Happens When Thifensulfuron Methyl is Introduced Into the Environment?

Thifensulfuron methyl poses a potential risk to terrestrial and aquatic plants, therefore, additional risk reduction measures must be observed.

When thifensulfuron methyl is released into the environment some of it can be found in soil and surface water. However, thifensulfuron methyl is rapidly broken down by soil microbes and by chemical reaction in water and thus is not expected to persist in the environment. Its major transformation products will be present in soil and aquatic systems for a longer period of time. Laboratory studies indicate that thifensulfuron methyl and its transformation products are mobile in soil. However, there is no field evidence that the use of this herbicide will result in groundwater contamination, most probably due to the rapid microbiological breakdown of thifensulfuron methyl in soil.

When thifensulfuron methyl is used for weed control in crops, there is a potential that nontarget plant species on land and in water may be exposed to the chemical as a result of spray drift or runoff. Some plant species are sensitive to the chemical and would be adversely affected. To minimize the potential exposure, strips of land between the agricultural field and the nontarget terrestrial or aquatic areas will be left unsprayed. The width of these buffer zones will be specified on the product label. Water monitoring data indicate that thifensulfuron methyl can occur in runoff. Thifensulfuron methyl presents negligible risk to wild birds and mammals, bees and other arthropods as well as to aquatic organisms like fish, amphibians and invertebrates.

Value Considerations

What is the Value of Thifensulfuron Methyl?

Thifensulfuron methyl controls a wide spectrum of broadleaf weeds in several major crops.

Thifensulfuron methyl reduces a portion of the economic losses caused by weeds (estimated at $432 million in the early 1990s for cereal crops, soybean, tomato, and forage grass for seed production). The application rate of thifensulfuron methyl is much lower (10 to 100 times) than alternative non-sulfonylurea broadleaf herbicides registered for use on the same sites, contributing to less chemical load in the environment. Thifensulfuron methyl can be tank mixed with a variety of herbicides and is known for its prepackaged tank mixes. The use claim for thifensulfuron methyl on imazethapyr tolerant canola and sufonylurea tolerant soybeans may provide an option to deal with emerging resistant weed problems arising from the current widely used herbicide-tolerant crop

systems, or a useful precedent for future development of herbicide tolerant crop systems. However, resistance management must be considered as more weed species are reported to be resistant to herbicides that inhibit acetolactate synthase (such as thifensulfuron methyl) than to herbicides having other modes of action.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of thifensulfuron methyl, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- To protect mixer/loader/applicators: additional protective equipment
- To protect workers re-entering treated sites: a restricted-entry interval
- To avoid drift to areas of human habitation or areas of human activity: precautionary statements
- To protect workers using wettable granular and soluble formulations: additional precautionary statements and directions for use

Environment

- To protect non-target terrestrial and aquatic plants: additional precautionary statements and changes to label statements as well as buffer zones for terrestrial and aquatic plants
- To reduce the potential runoff of thifensulfuron methyl to adjacent aquatic habitats: caution statements for the use on sites with characteristics that may be conducive to runoff when heavy rain is forecasted

Next Steps

Before making a re-evaluation decision on thifensulfuron methyl, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision document, which will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

At the time of the re-evaluation decision, registrants will be asked to submit the following supplementary information to confirm or refine the current risk assessment.

Other Information

When the re-evaluation decision is made, the PMRA will publish an Evaluation Report on thifensulfuron methyl in the context of this re-evaluation decision (based on the Science Evaluation Section of this consultation document). In addition, the test data on which the decision is based will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

SCIENCE EVALUATION

1.0 Introduction

Thifensulfuron methyl is a selective systemic herbicide. It belongs to the sulfonylurea chemical family and is classified as a Group 2 herbicide. The herbicidal activity of thifensulfuron methyl is due to the inhibition of the plant enzyme acetolactate synthase (ALS), also called acetohydroxyacid synthase (AHAS).

Following the re-evaluation announcement for thifensulfuron methyl, E.I. du Pont Canada Company, the registrant of the technical grade active ingredient (TGAI) and primary data provider in Canada, indicated it would continue to support all uses included on the label of Commercial Class end-use products. There are no Domestic Class end-use products containing thifensulfuron methyl registered in Canada.

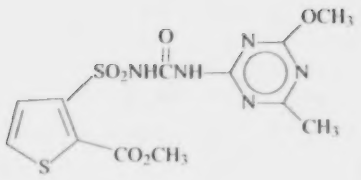
In addition to the PMRA reviews, the PMRA used recent assessments of thifensulfuron methyl from the United States Environmental Protection Agency (USEPA) and the European Union (EU). Information on the regulatory status of thifensulfuron methyl in the United States can be found on the USEPA's website at www.epa.gov/pesticides/op/status.htm. A summary of the EU evaluation of thifensulfuron methyl (and other pesticides) is available at http://ec.europa.eu/food/plant/protection/evaluation/exist_subs_rep_en.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Thifensulfuron methyl
Function	Herbicide
Chemical family	Sulfonylurea
Chemical name	
1. **International Union of Pure and Applied Chemistry (IUPAC)**	3-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoylsulfamoyl)thiophen-2-carboxylate
2. **Chemical Abstracts Service (CAS)**	3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]-2-thiophenecarboxylate
CAS Registry Number	79277-27-3
Molecular formula	$C_{12}H_{13}N_5O_6S_2$
Molecular weight	387.4

Structural formula



PCP Number: 21060

Purity: 98.0% (limits: 95.06 - 100.0%)

Basic Manufacturer: DuPont Agricultural Products Caribe Ltd.
Manati Plant, Manati, Puerto Rico

Identity of impurities of human health or environmental concern:

Based on the manufacturing process and the raw materials used, the product is not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, Appendix II.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Henry's law constant	4.4×10^{-10} Pa m^3 mol^{-1}
Vapour pressure at 25°C	1.7×10^{-5} mPa
Ultraviolet–visible spectrum	Not expected to absorb UV at $\lambda > 300$ nm
Solubility in water at 25°C	pH 5: 230 pH 7: 6270
n-Octanol–water partition coefficient (K_{ow})	pH 5: log K_{ow} 0.20 pH 7: log K_{ow} 0.02
Dissociation constant at 25°C (pKa)	pKa = 4.0

2.3 Description of Registered Thifensulfuron Methyl Uses

Appendix I lists all thifensulfuron methyl products that are registered under the authority of the *Pest Control Products Act*, specifically including one technical active ingredient, three manufacturing concentrates, and six Commercial Class end-use products. Three of the Commercial Class end-use products contain thifensulfuron methyl alone while the remaining are co-formulated with tribenuron methyl (two products) or chlorimuron ethyl (one product).

Appendix II lists all the uses for which thifensulfuron methyl is presently registered. All uses were supported by the registrant at the start of the re-evaluation and were, therefore, considered in the health and environmental risk assessments. Also presented is whether any of the uses were added through the PMRA minor use program. While currently supported by the registrant, the data supporting these minor uses were originally generated by a user group.

It should be noted that thifensulfuron methyl is also registered for tank-mixing with a wide range of other herbicides, most notably as prepackaged tank mixes with Group 1 herbicides (for grassy weed control).

Uses of thifensulfuron methyl belong to the following use site categories: terrestrial food crops, terrestrial feed crops, industrial oilseed crops and fibre crops. The crops specifically include wheat (spring, winter, and durum), barley, oats, flax (CDC Triffid), soybean, field tomato, forage grasses for forage and seed production (seedling or established), imazethapyr tolerant canola, and sulfonylurea tolerant soybean.

3.0 Impact on Human and Animal Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels where no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species. The health effects noted here were observed in animals at dose levels at least 100-fold (often much higher) above levels to which humans are normally exposed through use of products containing thifensulfuron methyl.

3.1 Toxicological Summary

The toxicology database supporting thifensulfuron methyl is primarily based on studies from the technical registrant. In laboratory animals, thifensulfuron methyl is of low acute toxicity by the oral and inhalation routes of exposure in the rat, of low acute toxicity by the dermal route of exposure in the rabbit, slightly irritating to rabbit skin, minimally irritating to rabbit eyes, and a non-sensitizer in Guinea pigs. Signs of acute toxicity, induced by very high doses of thifensulfuron methyl, are weight loss, diarrhea, yellow-stained perineal area and nasal discharge.

After oral exposure, absorption of thifensulfuron methyl was rapid (low doses) to moderate (high doses) with more than half of the administered dose excreted within the first 24 to 48 hours and more than 90% within 48 to 72 hours. Accumulation within tissues was minimal, with 41–92% of the administered activity recovered from the urine, and 10–31% recovered from the feces. The main component was the parent compound. A number of minor metabolites were found in the urine and in the feces including thifensulfuron methyl acid, O-demethyl thifensulfuron methyl and triazine amine.

In both short- and long-term studies the major effect was a reduction in body weight and body-weight gain, combined with increases in relative organ weights. No biologically significant effects were noted in the subchronic mouse study when tested at the limit dose. In the 90-day rat study, in addition to reduced body weight and body-weight gain, there were increases in relative brain, kidney and testes weight in males, and increases in brain and heart weight in females. In the dog, there were reduced body weight or body-weight gains in both a 13-week and 1-year study.

In the mouse oncogenicity study, in addition to a reduction in body weight and an increase in relative brain weight, there was an increased incidence of hepatocellular adenomas in males. The incidence of these tumours was close to, or within, historical controls, except at the high dose, which exceeded the maximum recommended dose of 1000 mg/kg bw/day. Therefore, this tumour type was not considered compound-related. In the chronic rat study there was a reduction in body-weight gain and a reduction in serum sodium concentration. There was an increase in adenocarcinomas of the mammary glands, but this does not appear treatment-related based on the following considerations:

i) the increase in incidence was not statistically significant
ii) mammary adenocarcinomas are a common tumour in aging rats
iii) the concurrent controls had an increased mean number of tumours that is higher than the mean in historical control data, indicating that the overall incidence of mammary adenocarcinoma was generally higher in this study
iv) there was no treatment-related increase in the incidence of non-neoplastic or pre-neoplastic lesions of the mammary gland
v) there were no mammary tumours in any animals sacrificed at 12 months, nor was there any indication of a decrease in latency period
vi) the tumours were only observed in one species (rat) and one sex (female)
vii) thifensulfuron methyl is not genotoxic.

In a developmental rat toxicity study, the incidence of absent or small renal papillae at the highest dose was greater than in historical controls and was considered treatment- related. The absence of renal papillae is considered a malformation which indicates teratogenicity, while small renal papillae are considered a developmental variation. A decrease in fetal body weight was also considered treatment-related. Since no adverse effects were noted in the dams, these effects indicate a fetal sensitivity. In the rabbit developmental toxicity study, a reduction in maternal body weight occurred at the highest dose tested, but no treatment-related effects were noted on

development. In a 2-generation reproductive study in the rat, a reduction in body weight occurred in F_0 females at termination. No effects were seen on reproductive or offspring parameters.

Reference doses have been set based on the NOAELs for the most sensitive indicator of toxicity, namely decreases in body-weight gain and reduced serum sodium in adult rats, and an increased incidence of absent renal papillae and small renal papillae in fetal rats. Reference doses incorporate uncertainty factors to account for extrapolating between laboratory animals and humans and, where required, a safety factor to account for fetal sensitivity.

The toxicology profile and toxicology endpoints used in the risk assessment of thifensulfuron methyl are summarized in Appendix III and IV.

3.2 Occupational and Non-Occupational Risk Assessment

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant NOAEL from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE which incorporates safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects. However, MOEs less than the target MOE require measures to mitigate risk.

3.2.1 Toxicological Endpoints

To estimate the risk from short-term (1–30 days) oral, dermal and inhalation exposure, an oral NOAEL of 25 mg/kg bw/day from a two-year chronic toxicity/carcinogenicity rat study at 90 days was used. The NOAEL by day 90 of the study was based on decreased body-weight gain at a LOAEL of 125 mg/kg bw/day. A target MOE of 100 is based on the standard uncertainty factors of 10 for interspecies extrapolation and 10 for intraspecies variability. An additional safety factor to account for fetal sensitivity was not considered necessary in the short-term risk assessment since the NOAEL selected (25 mg/kg bw/day) is inherently protective of the developmental sensitivity that has a NOAEL of 159 mg/kg bw/day.

To estimate the risk from intermediate-term (1–6 months) oral, dermal and inhalation exposure, an oral NOAEL of 5 mg/kg bw/day from the combined results of a two-year chronic toxicity/carcinogenicity rat study and a 90-day rat study was used. The NOAEL was based on decreased body-weight gain at six months. The LOAEL was 25 mg/kg bw/day. A target MOE of 100 is based on the standard uncertainty factors of 10 for interspecies extrapolation and 10 for intraspecies variability. An additional safety factor to account for fetal sensitivity was not considered necessary in the intermediate-term risk assessment since the NOAEL selected (5 mg/kg bw/day) is inherently protective of the developmental sensitivity that has a NOAEL of 159 mg/kg bw/day.

The PMRA does not consider thifensulfuron methyl to be carcinogenic, based on a weight-of-evidence approach.

Dermal Absorption
The PMRA can estimate dermal absorption by considering physical and chemical properties of a substance (e.g. molecular weight, log K_{ow} and solubility) and/or by considering chemical-specific dermal absorption data (e.g. in vivo rat dermal absorption study). Based on a first tier risk assessment, a default dermal absorption factor of 100% was used. No chemical specific dermal absorption data were available for the estimation of dermal absorption.

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to thifensulfuron methyl through mixing, loading and/or applying the pesticide, and when re-entering a treated site to conduct activities such as scouting and/or handling of treated crops.

Mixer/Loader/Applicator Exposure and Risk Assessment
There are potential exposures to mixers, loaders, applicators and other handlers. The following major exposure scenarios were assessed:

- Mixing and loading wettable or soluble granules.
- Mixing and loading wettable or soluble granules in water-soluble package (WSP).
- Applying by groundboom sprayer.

Occupational handlers of thifensulfuron methyl include farmers and custom agricultural applicators who mix, load and apply the herbicide. One application is permitted per season and based on the timing of application, the duration of exposure is expected to be short-term (1–30 days) for farmers and intermediate term (1–6 months) for custom applicators.

Exposure for all crop scenarios is predominantly dermal, with inhalation accounting for a minor component of overall exposure. The toxicological endpoint for these scenarios is based on an oral NOAEL. Because no dermal absorption study was available, the PMRA will use a default dermal absorption factor of 100% as a part of a first tier exposure risk assessment.

The PMRA estimated handler exposure based on the following level of personal protective equipment (PPE) :

Baseline PPE : Long pants, long-sleeved shirt and chemical-resistant gloves (gloves not required for groundboom sprayers).

Mixer/loader/applicator exposure estimates are based on the best available data at this time. The assessment might be refined with product-specific exposure data, biological monitoring data, and/or dermal absorption data.

No chemical specific exposure studies were available for use in the re-evaluation of thifensulfuron methyl. Thus, appropriate dermal and inhalation exposures were estimated using the Pesticide Handlers Exposure Database (PHED), Version 1.1. PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment.

In some cases, PHED did not contain appropriate data sets to estimate exposure to workers wearing additional PPE and/or using engineering controls, thus protection factors are applied for specific PPE and/or engineering controls. Surrogate data for wettable granules and soluble granules in WSP were not available in PHED, therefore closed mixing and loading data for wettable granules were used.

PHED unit exposures coupled with information on the amount of thifensulfuron methyl handled per day was used to estimate handler exposure. The amount handled per day is based upon the maximum label application rate and default assumptions on the area (of crop) which can reasonably be treated in one day.

Calculated MOEs exceed the target MOE for all exposure scenarios and are summarized in Appendix V, Table 1.

Postapplication Worker Exposure and Risk Assessment

Workers who re-enter treated sites to conduct activities involving foliar contact may be exposed to thifensulfuron methyl. Based on the crops and their associated re-entry activities, exposure to thifensulfuron methyl is expected to be short-term (1 to 30 days) in duration. One application per crop per season is expected (as per product labels) and post-application exposure may occur from scouting, thinning, hand pruning, hand harvesting, hand weeding, staking, tying, training, and irrigation of treated crops.

Default dislodgeable foliar residue (DFR) values and activity specific transfer coefficients (TC) were used to estimate postapplication exposure resulting from contact with treated foliage at various times after application. DFR data represent the amount of residue that can be dislodged or transferred from a treated surface, such as the leaves of a plant. In this case, no DFR studies were submitted, therefore, a default peak default DFR value of 20% of the application rate with 10% dissipation per day was used. A TC represents the amount of foliar contact per unit time and it relates worker exposure, to dislodgeable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples, scouting late-season cotton) and reflect standard agricultural work clothing worn by adult workers.

The postapplication risk estimates include a number of conservative inputs, such as the assumption that workers are exposed to residues following the maximum application rate.

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before one can safely re-enter. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in an MOE that is above the target MOE. Calculated MOEs exceed the target MOE on day 0, and proposed REIs are set at 12 hours. Results of the post-application exposure risk assessment for each potential use scenario are summarized in Appendix V, Table 2.

3.2.3 Non-occupational Exposure and Risk Assessment

3.2.3.1 Residential Handler Risk

There are no domestic class products registered in Canada; therefore, a residential handler risk assessment was not required.

3.2.3.2 Bystander Exposure and Risk

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible, thus, a bystander exposure risk assessment was not required.

3.3 Dietary Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to thifensulfuron methyl from treated imports is also included in the assessment. These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body-weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when risk exceeds 100% of the reference dose. PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute and chronic risk assessments procedures.

Residue estimates used in the dietary risk assessment (DRA) may be conservatively based on the maximum residue limits (MRL) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program (PDP).

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™ Version 2.03), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendix VI and VII.

3.3.1 Determination of Acute Reference Dose

An acute (1 day) reference dose (ARfD) was not calculated for the general population since there was not an acute endpoint of concern. For the population subgroup females 13+ an ARfD was calculated based on a NOAEL of 159 mg/kg bw/day from a developmental toxicity study in rats. The endpoint selected was based on increased incidences of absent renal papillae and small renal papillae at a LOAEL of 725 mg/kg bw/day. Standard uncertainty factors of 10 for interspecies extrapolation and 10 for intraspecies variability were used with an additional safety factor of 3 to account for sensitivity of the young, resulting in an ARfD of 0.53 mg/kg bw (159 mg/kg bw/day ÷ 300).

3.3.2 Acute Dietary Exposure and Risk Assessment

Acute dietary risk is calculated using the highest ingestion of thifensulfuron methyl likely on any one day, and using food consumption and food residue values. A statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of thifensulfuron methyl residue that might be consumed in a day. A value representing the high end (99.9th percentile) of this distribution is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is considered acceptable.

The acute potential daily intake at Tier I was minuscule and accounted for less than 0 .1 % (at the 95th percentile) of the ARfD for Female 13^{+} sub-populations and is, therefore, not of concern.

3.3.3 Determination of Acceptable Daily Intake

The acceptable daily intake (ADI) is the dose that an individual can be exposed to over the course of a lifetime and expect no adverse health effects. The ADI selected for thifensulfuron methyl was based on the NOAEL of 1.25 mg/kg bw/day from a 2-year chronic toxicity/carcinogenicity rat study The endpoint selected was based on decreased body-weight gain in the male and reduced serum sodium concentration at a LOAEL of 25 mg/kg bw/day. An overall uncertainty factor of 100 was required to account for interspecies extrapolation (10-fold) and intraspecies variability (10-fold), resulting in an ADI of 0.0125 mg/kg bw/day (1.25 mg/kg bw/day ÷ 100). This value was considered protective of all populations, including infants, children and females of childbearing age (13–49 years).

3.3.4 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is acceptable.

The chronic potential daily intake accounted for less than 5% of the ADI for all sub-populations and is, therefore, not of concern.

3.3.5 Cancer Potency Factor

A cancer potency factor was not established as the thifensulfuron methyl database did not suggest any carcinogenic potential in mice or rats.

3.3.6 Carcinogenic Dietary Exposure and Risk Assessment

A cancer risk assessment was not conducted as the thifensulfuron methyl database did not suggest any carcinogenic potential in mice or rats.

3.4 Exposure From Drinking Water

3.4.1 Concentrations in Drinking Water

Thifensulfuron methyl residues in potential drinking water sources were estimated using computer simulation models. The acute and the chronic estimated drinking water concentration values used in the exposure model are 1.27 ppb and 0.22 ppb, respectively.

3.4.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure was calculated using acute and chronic drinking water EEC values directly into DEEM-FCID™ Version 2.03.

Acute and chronic drinking water exposures are not of concern.

3.5 Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation).

Aggregate risk assessment looks at the combined potential risk associated with food, drinking water and residential exposures. Acute aggregate risk assessments do not combine residential and dietary exposures, as it is unlikely that an individual would be exposed to high-end dietary and residential exposure on the same day. For thifensulfuron methyl, acute aggregate exposure is, therefore, from dietary and drinking water exposures (see Section 3.3 and Section 3.4).

As residential use of thifensulfuron methyl is not permitted, the short-term aggregate exposure is comprised of contributions from food and drinking water. The relevant duration of exposure to assess toxicological endpoints for this assessment would be a period of up to one month. To estimate the risk from short-term exposure by all routes, a NOAEL of 25 mg/kg bw/day from a 2-year rat study at 90-days, based on decreased body-weight gain at 125 mg/kg bw/day, was selected. The 90-day rat study had a greater range between NOAEL and LOAEL (5 mg/kg bw/day vs. 125 mg/kg bw/day) than the 2-year study (25 mg/kg bw/day vs. 125 mg/kg bw/day), making the 2-year study at 90-days more appropriate for dose selection. The target MOE selected for the aggregate assessment is 100, comprised of the standard uncertainty factors of 10-fold for interspecies extrapolation and of 10-fold for intraspecies variability.

There are no registered residential uses for thifensulfuron methyl. Aggregate exposure and risk assessment from food and drinking water was not of concern.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Based on its physical-chemical properties (Section 2.2), thifensulfuron methyl is very soluble in water, is not likely to volatilize from moist soil or water surfaces under field conditions, and is not likely to bioaccumulate in organisms. Environmental fate data for thifensulfuron methyl are summarized in Appendix X, Table 1. Thifensulfuron methyl is relatively labile and dissipates from soil and aquatic systems by hydrolysis and biotransformation. At cooler temperatures the dissipation of thifensulfuron methyl is slower in all environmental media. Phototransformation is an important route of transformation for thifensulfuron methyl in water and air (Appendix IX). The major transformation products thifensulfuron acid, triazine amine, O-desmethyl thifensulfuron acid, 2-acid-3-sulfonamide and triazine urea are generally more persistent than thifensulfuron methyl. Water/sediment studies demonstrated that the majority of the applied radioactivity (60–70%) is preferentially associated with the water. All transformation products were very polar and were largely associated with the aqueous phase. There was no evidence of significant accumulation of either parent compound or its transformation products in the sediment.

Laboratory studies on adsorption/desorption and soil column leaching indicate that thifensulfuron methyl and its transformation products have a potential to be mobile in a variety of soils. Thifensulfuron methyl and its transformation products met all criteria identifying them as leachers. In contrast, field studies conducted in Canada and the United States detected thifensulfuron methyl and its transformation products in only the top 30-cm deep soil layer. Most probably leaching is offset by microbial degradation. Canadian water monitoring data have shown detections in surface water but not in groundwater.

4.2 Effects on Non-target Species

An assessment of environmental risk integrates the exposure and ecotoxicology data to estimate the potential for adverse ecological effects. Exposure is reflected in the calculation of initial and cumulative estimated environmental concentrations (EEC) in soil, water and wildlife food sources. These calculations are performed using a range of application rates selected from the supported uses taking into consideration the maximum number of applications and minimum interval between applications. Cumulative EECs are estimated by further adjusting the sum of the applications for dissipation between applications using the time for 50% decline (DT_{50}) from the appropriate environmental media.

A screening-level risk assessment is initially performed using the EECs for a direct overspray scenario. The environmental risk is characterized using the quotient method. A risk quotient (RQ), which is the ratio of the EEC to the most sensitive endpoint, is determined. The RQ = 1 is the level of concern (LOC). If the screening-level assessment indicates negligible risk (RQ less than 1), then no further assessment is done. However, if the screening-level assessment results in a potential risk (RQ greater than 1), then a refined assessment is undertaken for the organisms of concern. Refinement of the risk assessment takes into consideration more realistic exposure scenarios (e.g. drift to non-target habitats and runoff to water bodies) and may consider different toxicity endpoints. Data derived from monitoring studies may also be used in refining a risk assessment (Appendix VIII).

4.2.1 Effects on Terrestrial Organisms

A risk assessment of thifensulfuron methyl to terrestrial organisms was based on an evaluation of toxicity data on thifensulfuron methyl to earthworms (acute contact), bees (acute oral and chronic), four species of predatory and/or parasitic invertebrates, two species of birds (acute oral, dietary, and chronic), three species of mammals (acute oral, dietary, and chronic), and 10 species of terrestrial plants (seed germination, seedlings emergence and vegetative vigour). A summary of terrestrial toxicity data for thifensulfuron methyl are presented in Appendix X, Table 2. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with thifensulfuron methyl.

Thifensulfuron methyl demonstrated no adverse toxicological effects on terrestrial invertebrates, birds or mammals on an acute oral, dietary and reproductive basis. As thifensulfuron methyl is a herbicide, adverse effects to non-target terrestrial plants are expected. Plant emergence and vegetative vigour studies conducted with 10 plant species indicated that, although the seeds of most plant species emerged successfully, plants did not follow normal growth patterns due to the ability of thifensulfuron methyl to inhibit the plant enzyme acetolactate synthase, hence stopping cell division and plant growth by blocking branched chain amino acid biosynthesis. No toxicity studies conducted with thifensulfuron methyl transformation products were available for review.

The screening level risk assessment indicated that exposure to thifensulfuron methyl does not pose a risk to terrestrial invertebrates, mammals and birds. Appendix X, Table 3 summarizes the risk assessment from thifensulfuron methyl to terrestrial organisms.

As would be expected, the herbicide thifensulfuron methyl poses a risk to non-target terrestrial plants. The LOC was exceeded by as much as 500 times. Less than 0.9% of the thifensulfuron methyl application rate (3.3–15 g a.i./ha) is expected to negatively affect non-target terrestrial plants (EC_{25} divided by the application rate). As a result, a refinement of the risk assessment was conducted taking into consideration the concentrations of thifensulfuron methyl that could be present in terrestrial habitat directly adjacent to the application field through drift of spray. Spray drift data for a medium ASAE droplet size, as is generally used in groundboom applications of herbicides, indicate that the maximum amount of spray that will drift one metre down wind from the point of application during spraying is 6%. Using this percent drift, the off-site EECs for thifensulfuron methyl were calculated. Based on this method of refinement, thifensulfuron methyl poses a reduced risk to non-target terrestrial plants directly adjacent to the application field. Exceedance of the LOC was reduced to 30 times from 500 times. Buffer zones will be required to mitigate the risk of thifensulfuron methyl to non-target terrestrial plants. Appendix X, Table 4 summarizes the refined risk assessment from thifensulfuron methyl to non-target terrestrial plants.

4.2.2 Effects on Aquatic Organisms

Risk to aquatic organisms, acute and chronic, is based on an evaluation of toxicity data on thifensulfuron methyl for eight freshwater species (one invertebrates, three fish, two algae, one diatom, and one vascular plant) and one estuarine/marine species (algae). Some toxicity data on the transformation products were also available. A summary of aquatic toxicity data for thifensulfuron methyl and its transformation products is presented in Appendix X, Table 2. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with thifensulfuron methyl.

Thifensulfuron methyl and its transformation products are not toxic to freshwater invertebrates and fish on an acute bases. Chronic effects to freshwater fish and invertebrates are not expected. No chronic toxicity data were available for estuarine/marine species. As thifensulfuron methyl is a herbicide, adverse effects to non-target aquatic plants are expected. Thifensulfuron methyl affected biomass and cell density of freshwater and marine/estuarine algae. Thifensulfuron methyl significantly affected frond density and biomass of duckweed. The transformation products did not adversely affect algae or duckweed at the maximum concentrations tested.

The risk assessment was conducted using data for the most sensitive freshwater organisms tested *Daphnia magna*, bluegill sunfish (*Lepomis macrochirus*) and rainbow trout (*Oncorhynchus mykiss*), diatom (*Navicula pelliculosa*) and duckweed (*Lemna gibba)* as well as marine/estuarine algae *(Skeletonema costatum)*.

The screening level risk assessment indicated that thifensulfuron methyl does not pose a risk to freshwater invertebrates, fish, amphibians (based on surrogate data from fish studies) and algae. However, a potential risk to vascular plants was identified at the maximum application rate. The LOC was exceeded by 3.8 times at the application rate of 15 g a.i./ha. Thus, a refined risk assessment was triggered which reduced the exceedance of the LOC to less then 1 from spray drift and to 1.5 times from runoff. Additional risk mitigation measures are also required on the label. Risk assessment from transformation products was also conducted assuming that EEC for transformation products is the same as for the parent thifensulfuron methyl. Appendix X, Tables 5 and 6 summarize risk assessment from thifensulfuron methyl and its transformation products to aquatic organisms. Appendix X, Tables 7 and 8 summarize refined risk to aquatic plants from thifensulfuron methyl spray drift and runoff, respectively. As monitoring data were limited, they were not considered in the risk assessment.

5.0 Value

5.1 Commercial Class Products

All thifensulfuron methyl uses are supported by the registrant. There are no risk concerns for any of the registered uses. Consequently, no alternatives to the use of thifensulfuron methyl is considered.

5.2 Domestic Class Products

There are no Domestic Class products containing thifensulfuron methyl registered in Canada.

5.3 Value of thifensulfuron methyl

Weeds cause major losses in crop production. In Canada, the estimated average annual losses caused by weeds (in the early 1990s) were $291 million in wheat, $74 million in barley, $27 million in oats, $31 million in soybean, $5 million in tomato and $4 million in forage grass for seed production. Thifensulfuron methyl was reported to be used in these crops to prevent and reduce a portion of the economic losses caused by broadleaf weeds. In particular, thifensulfuron methyl is one of the leading postemergent broadleaf herbicides used in cereal crops (wheat, barley, and oats) in western Canada and is the only postemergent broadleaf herbicide registered for use on field tomato.

Thifensulfuron methyl is also registered for tank mixing with a wide range of other herbicides, most notably as prepackaged tank mixes with Group 1 herbicides, (for grassy weed control). These tank mixtures or prepackaged tank mixes broaden the weed control spectrum, resulting in a reduction in the number of application passes, soil compaction and costs to growers.

Due to the widespread and frequent use of ALS inhibiting (Group 2) herbicides and lack of rotation with herbicides with other modes of action, more resistant weed biotypes have been documented in Canada with Group 2 herbicides than with any other herbicide groups, including 12 broadleaf weeds (cleavers, chickweed, hemp-nettle, kochia, lamb's-quarters, giant ragweed, ball mustard, wild mustard, redroot pigweed, Russian thistle, spiny annual sowthistle, and stinkweed) and two grassy weeds (green foxtail and wild oats). Consideration has to be given to the development of herbicide resistance in weeds associated with the use of thifensulfuron methyl. Nevertheless, thifensulfuron methyl still plays a role in mitigating development of resistance in weeds to other herbicide groups. Currently available postemergence broadleaf herbicides for use in cereal crops are predominately Group 4 herbicides (synthetic auxins) and some Group 6 herbicides (inhibitors of photosynthesis at photosystem II site B). Thifensulfuron methyl is the only Group 2 postemergent broadleaf herbicide for use in cereal crops, thereby, playing a role in the rotation of herbicide groups.

Currently, thifensulfuron methyl is not used commercially on imazethapyr-tolerant canola and sulfonylurea-tolerant soybeans. However, this use claim may provide a potential option to deal with emerging resistant weed problems arising from the current widely used herbicide-tolerant crop systems, or a useful precedent for future development of herbicide-tolerant crop systems.

6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal Toxic Substances Management Policy (TSMP), which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, thifensulfuron methyl was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of thifensulfuron methyl were also considered, including major transformation products formed in the environment, microcontaminants in the technical product and formulants in the end-use products. The PMRA has reached the following conclusions:

- The *n*-octanol–water partition coefficient (log K_{ow}) of thifensulfuron methyl is 0.02, which is below the TSMP Track 1 cut-off criterion for log $K_{ow} \geq 5.0$. As well, thifensulfuron methyl does not meet the criteria for persistence as its half-life values in water (18–26 days) and soil (20 days) are below the TSMP Track 1 cut-off criteria for water (≥182 days), sediment (≥182 days) and soil (≥182 days).

Therefore, the use of thifensulfuron methyl is not expected to result in the entry of Track 1 substances into the environment.

6.1 Formulant Issues

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulant Policy and Implementation Guidance Document*. Published on 31 May 2006.

7.0 Summary

7.1 Human Health and Safety

7.1.1 Occupational Risk

The occupational application and postapplication risks are acceptable for the exposure scenarios involving the use of thifensulfuron methyl. The calculated margins of exposure for application and postapplication occupational exposures are all above the Agency's target assuming that workers wear baseline personal protective equipment.

7.1.2 Dietary Risk from Food

Acute and chronic dietary risk assessments demonstrate that there were no dietary concerns for any population subgroup in Canada, including infants, children, teenagers, adults and seniors. In addition, no dietary concerns were evident for nursing or pregnant females or based on gender in general.

7.1.3 Dietary Risk from Drinking Water

The potential for the contamination of drinking water with thifensulfuron methyl is expected to be negligible. There are no drinking water concerns for any population subgroup in Canada, including infants, children, teenagers, adults and seniors.

7.1.4 Residential Risk

There are no domestic uses of thifensulfuron methyl. Risks to homeowners from contact with commercially treated plants do not pose a health concern.

7.1.5 Aggregate Risk

Acute at < 0.1 % of the ARD and chronic at < 5 % of ADI aggregate exposure and risk from food and drinking water are not of health concern.

7.2 Environmental Risk

Thifensulfuron methyl is non-persistent in most soils and water systems, although its transformation products are more persistent than the parent compound. There is a potential that thifensulfuron methyl may appear in surface water through runoff. The risk assessment of thifensulfuron methyl indicates adverse effects on non-target terrestrial and aquatic plants. To reduce the effects of thifensulfuron methyl in the environment, mitigation in the form of precautionary label statements and buffer zones are required. Thifensulfuron methyl presents negligible risk to wild birds and mammals, bees and other arthropods as well as to aquatic organisms like fish, amphibians and invertebrates.

7.3 Value

Thifensulfuron methyl controls a wide spectrum of broadleaf weeds in several major crops.

Thifensulfuron methyl reduces a portion of the economic losses caused by weeds (estimated at $432 million in the early 1990s for cereal crops, soybean, tomato, and forage grass for seed production). Thifensulfuron methyl can be tank mixed with a variety of herbicides and is known for its prepackaged tank mixes. The use claim for thifensulfuron methyl on imazethapyr-tolerant canola and sufonylurea-tolerant soybeans may provide a potential option to deal with emerging resistant weed problems arising from the current widely used herbicide-tolerant crop systems, or a useful precedent for future development of herbicide-tolerant crop systems. However, consideration has to be given to resistance management as more weed species are reported to be resistant to herbicides that inhibit acetolactate synthase (such as thifensulfuron methyl) than to herbicides having other modes of action.

8.0 Proposed Re-evaluation Decision

The PMRA is proposing that thifensulfuron methyl is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and environment. As a condition of the continued registration of thifensulfuron methyl uses, new risk reduction measures must be included on the labels of all products. No additional data are being requested at this time.

8.1 Proposed Regulatory Action Related to Human Health

The PMRA has determined that the dietary and drinking water risks and the worker risks during mixing, loading and application are acceptable for all uses provided the mitigation measures listed in Appendix XI are implemented.

8.1.1 Residue Definition for Risk Assessment and Enforcement

Division 15, Table II, of the Food and Drug Regulations currently identifies the parent compound thifensulfuron methyl (methyl 3-(4-methoxy-6-methyl-1,3,5-triazin-2- ylcarbamoylsulfamoyl) thiophen-2-carboxylate) as the residue for risk assessment and enforcement. This residue definition is consistent with that of the USEPA.

8.1.2 Maximum Residue Limits for Thifensulfuron Methyl in Food

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to update Canadian maximum residue limits and to remove MRLs that are no longer supported.

As indicated in Table 8.1.2, the Food and Drug Regulations specify MRLs for thifensulfuron methyl residues in canola seed (imazethepyr-tolerant), flax seed (sulfonylurea-tolerant), soybeans (including STS soybeans) and tomatoes (field). Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specified MRL (i.e. wheat, barley, oats, corn, sorghum and rice) must not exceed the general MRL of 0.1 ppm.

Where no specific MRL for a pest control product has been established in the Food and Drug Regulations, subsection B.15.002(1) applies. This requires that residues do not exceed 0.1 ppm and has been considered a general MRL for enforcement purposes. Currently, residues of thifensulfuron methyl in all agricultural commodities, including those approved for treatment in Canada, are regulated by subsection B.15.002(1). However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*.

Extrapolation of available residue data for wheat, barley and oats and soybeans (including STS soybeans) following good agricultural practices (GAP), as described by the current product labels, indicated that residues would not exceed the limit of quantitation of the analytical method of 0.02 ppm (for wheat barley and oats) and 0.05 ppm (for soybeans including STS soybeans). If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set for wheat, barley, oats and soybeans (including STS soybeans).

Table 8.1.2 Thifensulfuron methyl MRLs for Commodities Approved in Canada

Commodity	MRL (ppm)
Barley grain	0.1*
Canola seed	0.02
Flax seed	0.02
Oat grain	0.1*
Soybean	0.1*
Tomato (field)	0.07
Wheat grain	0.1*

* By virtue of subsection B.15.002(1) of the Food and Drug Regulations, the maximum residue limit of foods for which MRLs have not specifically been established is 0.1 ppm.

List of Abbreviations

°C	degree(s) Celsius
a.i.	active ingredient
ADI	acceptable daily intake
AHAS	acetohydroxyacid synthase
ALS	acetolactate synthase
ARfD	acute reference dose
ASAE	American Society of Agricultural Engineers
atm	atmospheres
bw	body weight
CFIA	Canadian Food Inspection Agency
cm	centimetre(s)
DEEM®	Dietary Exposure Evaluation Model
DER	Data Evaluation Report
DFR	dislodgeable foliar residue
DNA	deoxyribonucleic acid
DT_{50}	dissipation time to 50% (the dose required to observe a 50% decline in the test population)
DWLOC	drinking water level of comparison
EC_{25}	exposure concentration to 25% (a concentration causing 25% adverse effects in the test population
EC_{50}	exposure concentration to 50% (a concentration causing 50% adverse effects in the test population
EChE	erythrocyte cholinesterase
EEC	expected environmental concentration
EXAMS	Exposure Analysis Modeling System
F_0	parental animals
F_1	first filial generation
g	gram(s)
GAP	good agricultural practice
GC-FPD	Gas Chromatography-Flame Photometric Detector
GC-MSD	Gas Chromatography-Mass Selective detector
GC-NPD	Gas Chromatography-Nitrogen Phosphorous Detector
h	hour(s)
ha	hectare(s)
Hg	mercury
IRED	Interim Reregistration Eligibility Decision (USEPA Document)
K_d	adsorption coefficient
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50% (a concentration causing 50% mortality in the test population
LD_{50}	lethal dose to 50% (a dose causing 50% mortality in the test population)

LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
LOEC	lowest observed effect concentration
m	metre(s)
m/sec	metre(s) per second
m^3	metre(s) cubed
mg	milligram(s)
µg	microgram(s)
mL	millilitre(s)
mm	millimetre(s)
MOE	margin of exposure
mv	millivolt(s)
MWHC	maximum water holding capacity
nd	no detection
NIO	nicosulfuron
nm	nanometre(s)
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
OC	organic carbon
OM	organic matter
PChE	plasma cholinesterase
PCP	Pest Control Product
PDP	Pesticide Data Program (United States data)
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PRZM	Pesticide Root Zone Model
PSI	pre-slaughter interval
Q_1^*	cancer potency factor
REI	restricted-entry interval
Rf	retardation factor in chromatography
RQ	risk quotient
TC	transfer coefficient
TGAI	technical grade active ingredient
TP	transformation product
TPM	triophanate-methyl
TSMP	Toxic Substances Management Policy
URMULE	User Requested Minor Use Label Expansion
US	United States of America
USEPA	United States Environmental Protection Agency
USGS NAWQA	United States Geological Survey National Water-Quality Assessment Program
wk	week

Appendix I Registered Thifensulfuron Methyl Products as of 27 June 2006

Registration Number	Marketing Class[1]	Registrant	Product Name	Formulation Type	Guarantee (%)[2]		
					MMM	MEX	CHE
21060	T	E.I. du Pont Canada Company	Thifensulfuron Methyl Technical Herbicide	Solid	98	—	—
21059	C		Refine Herbicide Dry Flowable	Wettable granules	75	—	—
21645	C		Plus Dry Flowable Herbicide (Component #1 of Triumph Plus)		75	—	—
22002	C		Pinnacle 75 Toss-N-Go Herbicide		75	—	—
22352	C		Refine Extra 75DF Herbicide		50	25	—
22575	C		Refine Extra Herbicide Toss-N-Go Bags		50	25	—
25444	M		Thifensulfuron Methyl 75DF		75	—	—
25457	M		Refine Extra MUP		50	25	—
25784	C		Reliance STS Toss-N-Go Herbicide		12	—	21
28144	M		Refine Extra 50SG MUP	Soluble granules	33.35	16.65	—

[1] T = Technical active; M = Manufacturing concentrate; C = Commercial.
[2] MMM = thifensulfuron methyl; MEX = tribenuron methyl; CHE = chlorimuron ethyl.

NOTE: Discontinued products or products with a submission for discontinuation are not included.

Appendix II Registered Uses of Thifensulfuron Methyl as of 27 June 2006[1]

Use-site Category	Site		Weeds[2]	Maximum Application Rate (g a.i./ha)	Supported Use?[3]
13, 14 Terrestrial feed and food crops	Wheat	Spring, winter and durum wheat - not underseeded to legumes or grasses	A	15	Y
			B	10 Plus tribenuron methyl at 5 (co-formulation)	
		Winter wheat (Ontario only)	B	10 Plus tribenuron methyl at 5 (co-formulation)	M
	Barley - not underseeded to legumes or grasses		A	15	Y
			B	10 Plus tribenuron methyl at 5 (co-formulation)	
	Oats - not underseeded to legumes or grasses		A	15	Y
			B	10 Plus tribenuron methyl at 5 (co-formulation)	
13 Terrestrial feed crops	Seedling or established grass species[4] for forage and seed production		B	10 Plus tribenuron methyl at 5 (co-formulation)	M
	Established grass species for forage and seed production - Kentucky bluegrass				
7 Industrial oilseed crops and fibre crops	Imazethapyr tolerant canola		A	15	Y
	Flax (CDC Triffid)				
	Soybeans		C	4.1	Y
			D	6	
	Sulfonylurea tolerant soybeans - Eastern Canada only		C	3.3	Y
			E	5.1	
14 Terrestrial food crops	Field tomatoes		C	4.1	M
			D	6	

[1] The formulation type for all supported end-use products is wettable granules. Application is made once per year by ground equipment only. No aerial application is allowed for any uses. Information on application equipment and the number of applications is based on both label use information and information provided by the registrant under DACO 5.2. Uses of tank mix products including the prepackaged tank mixes are not presented.

[2] A= Chickweed, hemp-nettle, lady's-thumb, redroot pigweed, corn spurry, Russian thistle, green smartweed, stinkweed, lamb's-quarters, cow cockle, wild mustard, wild buckwheat, volunteer rapeseed (non-imazethapyr tolerant canola), and kochia (suppression only for this weed)

B= WEEDS CONTROLLED: Annual smartweed (green smartweed, lady's thumb), ball mustard, chickweed, corn spurry, cow cockle, flixweed, common groundsel, hemp-nettle, kochia, lamb's-quarters, narrow-leaved hawk's-beard, redroot pigweed, Russian thistle, shepherd's purse, stinkweed, tartary buckwheat, volunteer rapeseed, volunteer sunflower, wild mustard, wild buckwheat
WEEDS SUPPRESSED: Cleavers (1 to 3 whorls), scentless chamomile, stork's-bill (2-6 leaf), round-leaved mallow, toadflax, Canada thistle, sow thistle

C= Redroot pigweed, wild mustard, lady's thumb

D= Redroot pigweed, wild mustard, lady's thumb, lamb's-quarters, velvetleaf

E= D plus common ragweed

[3] Y = Use is currently registered and supported by the registrant

M = Use was added as a User Requested Minor Use Label Expansion and is supported by the registrant.

[4] Forage grasses include meadow bromegrass, pubescent wheatgrass, smooth bromegrass, tall wheatgrass, creeping red fescue, slender wheatgrass, tall fescue, streambank wheatgrass, orchard grass, northern wheatgrass, crested wheatgrass, western wheatgrass and intermediate wheatgrass

Appendix III Toxicology Profile for Thifensulfuron Methyl

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise specified.

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Metabolism/Toxicokinetic Studies		
Metabolism of (thiophene-2-^{14}C) thifensulfuron methyl—CD rats		Absorption: - absorption appears rapid (low doses) to moderate (high doses) based on rates of excretion Distribution: - widely distributed - no accumulation - tissue and carcass in all cases < 0.7% of dose - highest concentrations in fat, skin, liver and kidney (lowest in brain, muscle and bone marrow); approximately 100-fold higher in high dose - each organ (except G.I. tract) contained less than 0.01% of the administered dose Metabolism: - little sex difference in the metabolism in any group - at least 9 metabolites in urine, 8 in feces (including parent compound) - parent constituted 88–96% of urine, 40–93% of fecal activity (70–75% of the total low dose groups) - in urine, 2-ester-3-sulfonamide, DPX-M6316 acid and thiophene sulfonamide were identified; 5 other unidentified metabolites could not be matched with reference standards. - in feces, 2-ester-3-sulfonamide, DPX-M6316 acid, thiophene sulfonamide and 2-acid-3-sulfonamide were identified; 3 other metabolites remained unidentified. - A metabolic pathway was proposed Excretion: - elimination of radioactivity was rapid: over half of the administered radioactivity was eliminated within 24 hours and more than 90% within 48 hours in the low dose groups (In the high dose group 50% of the radioactivity was eliminated by 48 hours and elimination was essentially complete by 72 hours). - by 96 hours less than 1% of the radioactivity was present in the tissues - Low dose: 71.0–75.9 % in urine; 9.6–15.7% in feces; 0.1–0.2% in carcass - Low dose preconditioned: 74.3–92 % in urine; 9.6–23.1% in feces - High dose: 41.2–69.6% in urine; 20.6% in feces

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Metabolism/Toxicokinetic Studies		
Metabolism of (triazine-2-^{14}C) thifensulfuron methyl—CD rats		Absorption: - absorption appears moderate based on rates of excretion [note: excretion rates were similar to the rates in the previous study at the same (high) dose] Distribution: - by 96 hours, the G.I. tract contained 0.01–0.09%; the skin 0.001–0.006%; liver 0.001–0.003; blood 0.002–0.004%; kidney 0.001–0.002% of the administered dose. - no effect of sex on tissue levels Metabolism: 92% of urine activity was parent compound (DPX-M6316) with 3 minor metabolites - DPX-M6316 acid, o-demethyl DPX-M6316 and triazine amine - DPX-M6316 in urine was 55.4 % (♂) and 72.0 % (♀) of administered dose; DPX-M6316 acid was 2.3 % (♂) and 2.5 % (♀) of administered dose with the other two metabolites at < 1% each - 84% (♂) and 77.8% (♀) of fecal activity was parent compound (DPX-M6316) with the 3 identified minor metabolites found in urine and 3 additional unidentified metabolites - DPX-M6316 in feces was 17.8% (♂) and 12.3% (♀) of administered dose; the 3 identified minor metabolites accounted for < 1.5% of the administered dose; 3 additional unidentified minor metabolites accounted for < 1.1% of the administered dose - a metabolic pathway was proposed Excretion: - 50% of the administered dose excreted by 48 hours; excretion was essentially complete by 72 hours - urinary activity ranged from 42.4–85.9 % in males and 56.5–86.6 % in females - fecal activity ranged from13.8–31.0 % in males and 12.6–20.9 % in females - expired CO_2 or volatiles was 0.01% in males and 0.03% in females

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Acute Toxicity Studies		
Acute oral toxicity—rat		LD_{50} >5000 mg/kg bw Signs: white crust seen on the external genitalia of several rats, diarrhea and yellow-stained perineum (1–3 days after dosing), ↓bw (1 ♂ - for 1 day after dosing) **LOW TOXICITY**
Acute dermal toxicity—rabbit		LD_{50} >2000 mg/kg bw Signs: none **LOW TOXICITY**
Acute inhalation toxicity—rat		LC_{50} >7.9 mg/L Signs: red ocular and nasal discharge, ↓bw (all animals day following exposure - ♂ test group slightly higher weight loss than controls) **LOW TOXICITY**
Eye irritation—rabbit		Mild conjunctival redness and slight chemosis (6/6) at 1 hr; slight corneal opacity and moderate iritis (1/6) at 1 hour; no corneal injury All ocular irritation resolved by 24 hr. Mean eye irritation score was 9.8 (range of 4–39) **MINIMALLY IRRITATING**
Dermal irritation—rabbit		Slight erythema in 5 rabbits by 4 hours (skin not evaluated at 1 hour post dose); by 24 hours all rabbits exhibited slight erythema with 2 rabbits displaying slight edema as well (MIS = 1.33). By 48 hours no dermal irritation was exhibited by any animal. **SLIGHTLY IRRITATING**
Dermal sensitization—Guinea pig		**NON-SENSITIZER**

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Subchronic Toxicity Studies		
90-day oral (feeding)—mouse	≥1125	no adverse effects at the highest dose tested
90-day oral (feeding)—rat	5	≥125 mg/kg bw/day: ↓bw [6.0%/9.8% (♂/♀)], ↓bw gain [8.3%/17.4%(♂/♀)], ↑rel. brain wt./bw (♂) 375 mg/kg bw/day: ↑rel. brain, kidney and testes wt./bw (♂), ↑rel. brain and heart wt./bw (♀) **Note**: In the 2-year rat study at 90 days the figures for bw/bw gain were the following: 25 mg/kg bw/day: ↓bw (♂-3.6%), ↓bw gain (♂-5.3%) 125 mg/kg bw/day: ↓bw [6.5%/3.0% (♂/♀)], ↓bw gain [9.4%/5.4%(♂/♀)] Weight reductions at 25 mg/kg bw/day were considered non-adverse. The NOAEL for the 2-year study at 90 day s was set at 25 mg/kg bw/day (see below).
90-day oral (feeding)—Beagle dog	37.5	187.5 mg/kg bw/day: ↓bw (♂ - slight), ↓bw gain (♂ - 56% of controls), ↑adrenal wt.(♂ - absol. and rel.)
1-year oral (feeding)—Beagle dog	18.75	187.5 mg/kg bw/day: ↓bw gain (♀), ↑liver/bw (♂)

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Chronic Toxicity/Oncogenicity Studies		
18-month feeding study —mouse	≥666	112.5 mg/kg bw/day: ↓bw (♀ at final weighing - 4.4%), ↑brain/bw (♀ - 4.7%), ↑incidence of hepatocellular adenomas (♂ - bordering on sig.)* 1,125 mg/kg bw/day: ↓bw (♀ at final weighing - 5.5%), ↓bw gains (♀ - 13.4%), ↑brain/bw (♀ - 6.4%), ↑ incidence of hepatocellular adenomas (♂)* *In 6 studies between 1980–1987 the incidences of hepatocellular adenomas in male control mice of this strain in 18-month feeding studies was 10% (range 5.4%–13.8%). In the present study, at 0, 3.75, 112.5 and 1,125 mg/kg bw/day, there were incidences of 11.3%, 11.3%, 15%, and 20% indicating a possible treatment-related effect at the mid and high dose. However, hepatocellular carcinomas decreased with treatment, i.e. at 0, 3.75, 112.5 and 1125 mg/kg bw/day there were 4/80, 4/80, 2/80, 3/80 respectively, the highest dose exceeded the recommended limit dose of 1000 mg/kg bw and the concurrent control also showed higher incidence of this type of adenomas. Therefore, the hepatocellular adenomas were not considered treatment related. Increase in brain/bw is probably a reflection of reduced bw **not carcinogenic**

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Chronic Toxicity/Oncogenicity Studies		
Two-year feeding study—rat	1.25	25 mg/kg bw/day (500 ppm): occasionally ↓bw (♂ - 3.0–4.6 % lower), ↓bw gain (♂ - sig. 0–182 days - 6.1 %), ↓serum Na^+ 125 mg/kg bw/day (2500 ppm): ↓bw [♂ - 2.5-7.2 % ↓ 0-379 days (slight but sig.); 3.9% ↓ for duration (not sig.)], occasionally ↓bw (♀ - 3.6–4.7 %), ↓bw gain (♂ - sig. 0–182 days - 9.1 %; ♀ - ↓ weight gains at 0–140 days only - 6.3 %), slight ↓food consumption (not sig.), ↓serum Na^+ **Note 1**: At 90 days the figures for bw/bw gain were the following: 25 mg/kg bw/day: ↓bw (♂-3.6%), ↓bw gain (♂-5.3%) 125 mg/kg bw/day: ↓bw [6.5%/3.0% (♂/♀)], ↓bw gain [9.4%/5.4%(♂/♀)] Weight reductions at 25 mg/kg bw/day were considered non-adverse. A NOAEL for the 2-year study at 90 days was therefore set at 25 mg/kg bw/day. This value was used in the calculation of the short-term oral, dermal and inhalation risk assessment **Note 2**: There was an increase in adenocarcinomas of the mammary gland at the two highest doses tested. However, thifensulfuron methyl is not considered carcinogenic or oncogenic based on the following information: i) the increase in incidence was not statistically significant (Fisher Exact test, with Bonferroni correction) ii) mammary adenocarcinomas are a common tumour in aging rats iii) the concurrent controls had an increased mean number of tumours that is higher than the mean in historical control data, indicating that the overall incidence of mammary adenocarcinoma was generally higher in this study iv) there was no treatment-related increase in the incidence of non-neoplastic or preneoplastic lesions of the mammary gland v) there were no mammary tumours in any animals sacrificed at 12 months, nor was there any indication of a decrease in latency period vi) the tumours were only observed in one species (rat) and one sex (female) vii) thifensulfuron methyl is not genotoxic **not carcinogenic**

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Reproductive and Developmental Toxicity Studies		
Two-generation reproduction feeding study— rat	Parental: 25 Offspring/Reproductive: >125	Parental: 125 mg/kg bw day: ↓bw (F_0 dams at weaning of F_{1b} - 9.0%), slightly ↓bw [F_{1b} parents - ♂(3.8%)/♀(5.5%) - not sig.] Reproductive/Offspring: no effects
Developmental study (gavage)— rat	Maternal: >725 Developmental: 159	Maternal: no adverse effects Developmental: 159 mg/kg bw/day: ↓# ♂ fetuses/litter (slight), microphthalmia (1 fetus) 725 mg/kg bw/day: ↓fetal bw (2.7% - slight, but sig.), ↓# ♂ fetuses/litter (slight), ↑incidence of absent renal papillae (not sig., 5 fetuses in 5 litters) and small renal papillae (sig., 4 fetuses in 4 litters), microphthalmia (2 fetuses - diff. litters) The significant reduction in the mean number of males/pregnant animal was not accompanied by a significant decrease in # live fetuses/pregnant animal, # resorptions/dam, or a significant increase in mean number of females/pregnant animal (at 0, 26, 159, 725 mg/kg bw/day there were 7.2/6.6, 6.6/6.9, 5.9**/7.3, 6.0*/7.4 ♂/♀ per pregnant dam). Therefore, this effect is not considered treatment-related. The occurrence of microphthalmia was within the range of historical control data - out of 15 studies (1983–1987, same lab), 4 had 1–2 fetuses and litters with microphthalmia. Therefore, this effect is not considered treatment-related. The incidence of absent or small renal papillae at 725 mg/kg (absent in 5 fetuses in 5 litters; small in four fetuses in four litters) was slightly higher than historical controls (in 9 studies conducted in 1983 and 1984, 6 had fetuses with absent papillae (range 1–3) and 5 had fetuses with small papillae (range 1–3). The absence of renal papillae is considered a malformation. This effect is treatment-related and adverse. **fetal sensitivity** **teratogenic**

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Reproductive and Developmental Toxicity Studies		
Developmental study (gavage)—rabbit	Maternal: 158 Developmental: >511	Maternal: ≥ 158 mg/kg bw/day: orange-tinted urine (during dosing) 511 mg/kg bw/day: ↓bw gain: 1.) days 7 to 9, first 2 days of dosing - at 0, 22, and 158 mg/kg bw/day, bw/rabbit increased 4.0g, 20.5g, and 11.7g respectively; at 511 mg/kg bw/day, bw/rabbit decreased 36.0 g. The reduction in bw for the 511 mg/kg bw/day group was significant at $p = 0.07$ 2.) days 7–20 - at 0, 22, 158, and 511 mg/kg bw/day, bw/rabbit increased 151.6g, 172.1g, 104.8g, and 88g respectively (not significant). Developmental: no treatment-related effects **No evidence of teratogenicity**
Genotoxicity Studies		
Ames reverse mutation test —*Salmonella typhimurium* TA1535, TA97, TA98, TA100	**Negative**	
In vivo micronucleus test - CD-1 mouse	**Negative**	
In vivo cytogenetics assay - CD rat bone marrow	**Negative**	
In vitro gene mutation assay—CHO/HGPRT cells	**Negative**	
In vitro unscheduled DNA synthesis assay—rat primary hepatocytes	**Negative**	

Appendix IV Toxicology Endpoints for Health Risk Assessment for Thifensulfuron Methyl

Exposure Scenario	Dose (mg/kg bw/day)	Endpoint	Study	UF/SF or MOE[a]
Acute dietary General Population	An acute reference dose was not calculated for the general population since there was not an endpoint of concern			
Acute dietary Females 13+	NOAEL = 159	Increased incidence of absent renal papillae and small renal papillae	Developmental study—rat	300 extra factor of 3 for fetal sensitivity and the presence of a malformation
	ARD = 0.53 mg/kg bw/day			
Chronic dietary	NOAEL = 1.25	Reduced body-weight gains in males, reduced serum sodium	2-year feeding study—rat	100
	ADI = 0.0125 mg/kg bw/day			
Short[b]-term oral, dermal and inhalation	NOAEL = 25	Decreased body-weight gain (90 days)	2-year feeding study at 90 days—rat	100
Intermediate[c]-term oral, dermal and inhalation[d]	NOAEL = 5	Decreased body-weight gain (6 months)	2-year feeding study combined with 90 day feeding study—rat	100
Cancer	non-carcinogenic			

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments, MOE refers to desired margin of exposure for occupational or residential assessments

[b] Duration of exposure is 1–30 days

[c] Duration of exposure is 1–6 months

[d] Because an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation

Appendix V Summary of Occupational Exposure Risk Estimates for Thifensulfuron methyl

Table 1 Route Specific MOEs for Mixers/Loaders/Applicators of Products Containing Thifensulfuron methyl.

Crop	Method of Application	Formulation[a]	Application Rate[b] (kg a.i./ha)	Area Treated per day (ha)	Margins of Exposure SHORT TERM (1–30days)			Margins of Exposure INTERMEDIATE TERM (1–6months)		
					Dermal[c]	Inhalation[d] (no respirator)	Combined[e]	Dermal[c]	Inhalation[d] (no respirator)	Combined[e]
Baseline PPE (see Section 3.2.2) : open M/L or closed M/L for WSP; open cab application without gloves.					**Taget MOE = 100**			**Target MOE = 100**		
Barley, Canola, Flax, Grass (forage/seed), Oats, Wheat (durum, spring, winter)	Groundboom	WG, SG	0.015	Farmer: 100	5930	589 226	5871	1186	117 845	1174
				Custom: 300	1977	196 409	1957	395	39 282	391
Barley, Grass (forage/seed), Oats, Wheat (durum, spring, winter)		WG (WSP), SG (WSP)		Farmer: 100	23 637	1 098 556	23 139	4727	219 711	4628
				Custom: 300	7879	366 185	7713	1576	73 237	1543
Soy beans		WG (WSP)	0.006	Farmer: 100	59 093	2 746 390	57 849	11 819	549 278	11 570
				Custom: 300	19 698	915 463	19 283	3940	183 093	3857
Tomatoes (field)		WG (WSP)		30	196 978	9 154 635	192 829	39 396	1 830 927	38 566

[a] WG = wettable granule, SG = soluble granule, WSP = water soluble package.

[b] Maximum label rate.

[c] Dermal MOE = dermal NOAEL / dermal exposure. Short-term NOAEL = 25 mg/kg bw/day and intermediate-term dermal NOAEL = 5 mg/kg bw/day. Dermal exposure (µg/kg bw/day) = (dermal unit exposure value × area treated per day × application rate × DA)/ body weight. DA (dermal absorption) = 100%. Body weight = 70kg.

[d] Inhalation MOE = inhalation NOAEL / inhalation exposure. Short-term NOAEL = 25 mg/kg bw/day and intermediate-term dermal NOAEL = 5 mg/kg bw/day. Inhalation exposure (µg/kg bw/day) = (Inhalation unit exposure value × area treated per day × application rate)/ body weight. Body weight = 70kg.

[e] Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$.

Table 2 Postapplication Exposure Estimates for Re-entry into Fields Treated with Thifensulfuron methyl.

Crop and Rate (kg a.i./ha)	Activity	Transfer Coefficient [a] (cm^2/hr)	Calculated DFR[b] at Day 0 (µg/cm^2)	Exposure [c] (µg/kg bw/day)	MOE [d] Target = 100
Barley, Canola (imazethapyr tolerant), Flax (CDC triffid), Grass (forage/seed), Oats, Wheat (durum, spring, winter) Rate: 0.015	Scouting, irrigation (full foliage)	1500	0.03	5.14	4 861
	scouting, irrigation (low foliage)	100		0.34	72 917
Soybeans Rate: 0.006	Scouting, irrigation (full foliage)	1500	0.012	2.06	12 153
	Hand weeding (full foliage), scouting (min. foliage)	100		0.14	182 292
Tomatoes (field) Rate: 0.006	Hand harvesting, hand pruning, staking, thinning, training and tying (full foliage)	1000		1.37	18 229
	Irrigation and scouting full foliage), hand pruning, staking and tying (min. foliage)	700		0.96	26 042
	Hand weeding (full and min. foliage), irrigation, thinning, scouting (min. foliage)	500		0.69	36 458

[a] Transfer coefficients (TC) are from the Science Advisory Council for Exposure, Policy No. 003.1 (USEPA, 2000b) and any amendments thereof.
[b] Dislodgeable foliar residue (DFR) calculations are based on a default peak DFR value of 20% of the application rate and a dissipation rate of 10 % per day. Based on one application per season.
[c] Exposure = DFR x TC x 8 hr x DA / 70 kg. (DA = dermal absorption of 100 %). [d] Based on worker short-term NOAEL of 25 mg/kg bw/day and target MOE of 100.
Margin of Exposure (MOE) = NOAEL/Exposure.

Appendix VI Summary of Dietary Risk Estimates for Thifensulfuron methyl

Table 1 Results of Tier 1 Deterministic Acute and Chronic Dietary Exposure and Risk Analysis for Thifensulfuron Methyl

Population Type	Acute Dietary Deterministic (95th Percentile)		Chronic Dietary	
	Exposure [3] (mg/kg bw/d)	Risk : % of ARD [1]	Exposure [3] (mg/kg bw/d)	Chronic Risk : % of ADI [2]
General Population	no toxicological endpoint of concern		0.000248	2
All infants (< 1 yr old)	"		0.000314	2.5
Nursing infants	"		0.000098	0.8
Non-nursing infants:	"		0.000396	3.2
Children 1–2 yrs	no toxicological endpoint of concern		0.000513	4.1
Children 3–5 yrs	"		0.000578	4.6
Children 6–12 yrs	"		0.000435	3.5
Female 13+ (pregnant/not nursing)	0.00047	0.09	0.000197	1.6
Female 13+ (nursing)	0.00051	0.1	0.000189	1.5
Youth 13–19 yrs	no toxicological endpoint of concern		0.000322	2.6
Females 13–19 (not preg or nursing)	0.00071	0.13	0.000278	2.2
Males 13–19 yrs	no toxicological endpoint of concern		0.000365	2.9
Adults 20–49 yrs	no toxicological endpoint of concern		0.000203	1.6
Females 20+ (not preg or nursing)	0.000442	0.08	0.000158	1.3
Males 20+ yrs	no toxicological endpoint of concern		0.000192	1.5
Females 13–49 yrs	0.00055	0.1	0.000201	1.6
Adults 50+ yrs	no toxicological endpoint of concern		0.000126	1

[1] Acute Reference Dose (ARD) Female 13+) = 0.53 mg/kg bw/day; There is no ARD for the general population; e.g of % Acute Risk Female 13+ (nursing) = acute Exposure/ARD × 100 = (0.000510/0.53) × 100 = 0.1%, see Table 1.

[2] Acceptable daily intake (ADI) = 0.0125 mg/kg bw/day; e.g of % Chronic Risk = Chronic Exposure/ADI × 100 = (0.000248/0.0125) × 100 = 2.0 %, see Table 1 for the chronic risk of the general population.

[3] Acute and Chronic Exposure = Consumption of food for each of the population sub-group (continuous survey of food intakes by individuals [CSFII] × residue exposure value in food consumed by that population sub-group.

Appendix VII Food Residue Chemistry Summary

1.1 Metabolism

1.1.1 Plant Metabolism

Metabolism studies have been reviewed by the PMRA for wheat and corn. The PMRA also reviewed US DERs and a summary of soybean metabolism study. All these metabolism studies indicated rapid absorption and degradation with total radioactivity at maturity of < 0.0005 ppm in cereal grains, < 0.02 ppm (limit of detection, LOD) in corn and < 0.0016 ppm in soybeans.

In a minor use submission for an expansion of use to tomatoes, the sponsor requested a waiver from any further metabolism studies. This was reviewed and accepted by the PMRA based on the following conclusions quoted below:

" no further plant metabolism studies are required based on the following:
1) the metabolism of thifensulfuron methyl was similar in corn, wheat and soybean,
2) the residues of thifensulfuron methyl in tomatoes are expected to be low (≤ 0.06 pm).
3) the metabolism of thifensulfuron methyl (corn, wheat and soybeans) and rimsulfuron (tomato)
were similar, i.e., both showed the concentration of TRRs declined rapidly, resulting in low residues in RAC."

The PMRA review based on the above rationale, waived the requirement for tomato metabolism study because the metabolism of thifensulfuron methyl was adequately understood in the other three representative crops (corn, wheat and soybean).

Insufficient data were noted in support of a chicory or another tuber crop metabolism study. As such, a chicory metabolism study or a metabolism study from a third diverse crop (listed in Crop Group 1 - Root and Tuber) is required to be submitted to the PMRA for a review. Residue definition (RD) based on the reviewed corn, wheat and soybean metabolism studies on file was defined as the parent, thifensulfuron methyl.

1.1.2 Livestock Metabolism

The PMRA has reviewed goat and hen metabolism studies. The goat and hen metabolic profile was the same as that of the rat metabolic profile as determined from the rat metabolism study. The PMRA reviews concluded that the RD defined in animals was the same as that for the plants, to be the parent, thifensulfuron methyl.

1.1.3 Residue Definition

MRLs for residues in or on food commodities are currently expressed in terms of the parent, thifensulfuron methyl (methyl 3-(4-methoxy-6-methyl-1,3,5-triazin-2- ylcarbamoylsulfamoyl) thiophen-2-carboxylate) [see Part B, Division 15, Table II of the *Food and Drugs Act* and Regulations *(FDAR)*].

1.2 Analytical Methods

1.2.1 Methods for Residue Analysis of Plants and Plant Products

Analytical method (AMR-1872-90) for analysis of thifensulfuron methyl residue in soybeans was reviewed by the PMRA This HPLC-UV method had a limit of quantitation (LOQ) of 0.02 ppm for residues of thifensulfuton methyl in soybean matrices. Recoveries within 70–120% at spiking levels ranging from 0.011 to 0.11 ppm in soybean matrices were satisfactory. UV detector response for thifensulfuron methyl was linear in soybean matrices with the range of 0.005–0.05 ppm. The review concluded that the method was acceptable; and also indicated that inter-laboratory validation (ILV) of the method was not submitted.

The proposition by the registrant that the method, AMR-1872-90 be considered as an enforcement method was reviewed by the PMRA. It concluded that the method could not be considered as an enforcement method until specificity of the method to quantitate thifensulfuron methyl in presence of tribenuron-methyl or any other sulfonylurea herbicides was demonstrated.

The PMRA reviewed a plant analytical method for thifensulfuron methyl residues in tomato samples using acetone and 0.1 M ammonium carbonate mixture (1:9 v/v) followed by filtration and solid phase clean-up (C_{18} SPE cartridge) prior to analysis using HPLC with UV detection and confirmation by HPLC-MS. Limit of detection (LOD) and limit of quantitation (LOQ) for thifensulfuron methyl residues was 0.005 ppm and 0.05 ppm, respectively. % recoveries for tomato samples spiked at 0.05 ppm, 0.10 ppm and 0.5 ppm were 99.5% (n=2), 97.0 ± 11.0% (n=3) and 95.0 ± 1.9% (n=5), respectively. The method had a good repeatability based on the standard deviations measured with respect to the recoveries at 2x LOQ. There was good linearity [coefficient of correlation = 0.99] for spiking level range of 0.10 to 10.0 ppm. Control tomato samples chromatogram spiked at the LOQ showed peak shape and sensitivity. The PMRA review indicated that potential positive samples be analyzed for confirmation by HPLC-MS as the HPLC-UV method could result in false positives due to many compounds that could be co-extracted during sample preparation and have the analyte with the same retention time (RT) and co-eluting (same RT) with the peak of interest.

The PMRA review concluded that the analytical method was valid and acceptable (accuracy, repeatability and reproducibility) and conforms with the RCGs (Residue Chemistry Guidelines, DIR98-02, Section 3.0).

Health Canada reviewed the analytical methods to measure the parent, thifensulfuron methyl residue in plant tissues (soybeans and tomatoes) and it appears to be satisfactory for enforcement purposes, based on the percentage of recovery and sensitivity of the method. LOQ in soybeans was 0.02 ppm and in tomatoes was 0.05 ppm, respectively.

1.2.2 Methods for Residue Analysis of Food of Animal Origin

Health Canada has reviewed a HPLC analytical method (reverse phase, RP) for determination of residue of the parent, thifensulfuron methyl in animal products. Limit of detection (LOD) in liver and kidney was 0.001 ppm, breast and thigh muscle was 0.002 ppm, and skin and fat was 0.004 ppm, respectively. The method appears to be satisfactory for enforcement purposes, based on the percentage of recovery and sensitivity of the method

1.2.3 Enforcement Method (DuPont Method No.:-5367 - Analytical enforcement method)

Method Validation

Detector Response- Standard solutions of thifensulfuron methyl for calibration of the detector ranged from concentration of 1.0 to 30.0 ppb. Relative standard deviation (RSD) for all samples analyzed for standard response factor was less than 20%.

Interferences - No detectable interferences were detected in control sample chromatograms at the retention time (RT) of thifensulfuron methyl.

Recoveries - Wheat (grain, forage and straw) samples were fortified with thifensulfuron methyl standard solution ranging from 0.01–0.10 ppm for wheat grain and 0.05–0.50 ppm for wheat forage and straw. Average percent recoveries with %RSD at each fortification level of thifensulfuron methyl is summarized below:

Matrix	Fortification Level (ppm)	Average Percent Recovery (± %RSD)
Wheat Grain	0.01 0.10	87% (±3) 98% (±2)
Wheat Forage	0.05 0.50	103% (±2) 102% (±3)
Wheat Straw	0.05 0.50	82% (±7) 90% (±3)

Recoveries for fortification range of 0.01–0.10 ppm for wheat grain and 0.05–0.50 ppm for wheat forage and straw of thifensulfuron methyl are acceptable.

Extraction Efficiency - was not conducted for thifensulfuron methyl per se in this study. However, extraction efficiency was demonstrated in a separate study employing a similar buffer extraction system with chlorsulfuron. Potassium phosphate buffer (30-mM) was used to extract [^{14}C]chorsulfuron residues in wheat and oats at 91.6–95.5% efficiency. Extraction efficiency for thifensulfuron methyl was not conducted because residue of the parent compound was not detected in treated wheat samples generated in the metabolism study. As thifensulfuron methyl residues has similar polarity and solubilities as chlorsulfuron, that would enable it to be extracted just as efficiently (91.6–95.5% efficiency).

Limit of Quantitation (LOQ) - was not determined during the course of this study. Instead, a bridging study was used to determine LOQ in wheat grain at 0.01 ppm and in wheat forage and straw at 0.05 ppm, respectively. At this fortification level, average recoveries ranged from 70–110% and RSD was at < 20%.

1.2.4 Multiresidue Analytical Methods

MRM was not reviewed as per information on file. Thifensulfuron methyl is not listed in the CFIA's list of MRMs (Vol #7, Pesticide Multi-Residue Methods Manual). The registrant (DuPont) submitted the MRM study (Method No.: Dupont AMR 877-87) for a review to Exposure Re-Evaluation Section - 2 (ERS-2). It was reviewed but was not satisfactory because thifensulfuron methyl, the RD did not give a sufficient response to be detected by the HPLC system.

Analysis Time
Twelve samples could be prepared during the course of a normal day. The equipment used in this study required about 50 minutes run per standard or sample. The run for analysis can be left unattended overnight. Confirmatory analysis required an additional day.

Method Ruggedness
Stability: All the stock solutions were in acetonitrile and stored in a freezer at 0 to −20°C was for at least one month. Standards aqueous solutions for calibration must be prepared daily. Extracted solutions were stable for 48 hours stored at 0 to −20°C. Standards for calibration must be prepared on the same day as the extracts.

Specificity and Potential Interferences: The method was tested for potential interferences from other sufonyl urea herbicides. The RT for thifensulfuron methyl (DPX-M6316) was distinctly resolved from other sulfonyl urea herbicides at 21.3 minutes; and there were no potential Interferences.

Conclusion

The PMRA evaluated the enforcement method (DuPont-5367) for data-gathering. It was adequately validated and acceptable for the quantitation of thifensulfuron methyl residues in wheat forage and straw matrices. In this study, GLP was not conducted because the USEPA FIFRA (40 CFR Part 160) GLP are not applicable to analytical methods. However, the analytical grain, procedures, documentation and archiving of the validation data were done following Standard Operating Procedures.

Independent Laboratory Validation study (ILV study, DuPont-8054) for method, DuPont-8054 was evaluated by the PMRA. The ILV was adequate to quantitate thifensulfuron methyl residues in wheat grain, forage and straw matrices for data-gathering and has been adequately validated. This method was conducted in compliance with the USEPA FIFRA (40 CFR Part 160), GLP standards, consistent with the OECD Principles of GLP.

1.3 Food Residues

1.3.1 Freezer Storage Stability

Freezer storage stability studies were reviewed for wheat grain, straw and green foliage (18 months at −20°C) and corn grain and forage (up to 2 years, "freezer conditions"). In another PMRA review, freezer storage stability of thifensulfuron methyl residues in wheat grain was three years, in wheat straw was two years, corn kernel and corn forage was two years each, respectively; and average thifensulfuron methyl residue recovery values for these crops were 78% in wheat, 84% in wheat straw, 95% in corn kernel and 93% in corn forage.

Tomato freezer storage study was not submitted with the residue data package. Therefore the review concluded that a freezer storage stability study was required for tomatoes or another crop within the fruiting vegetable crop group # 8, for a period of at least 7 months.

Level C1 preliminary review for deficiencies noted that freezer storage stability in animal matrices was not submitted. For any expansion, the review stated that for use to feed items, a feeding study would be required; until then the feeding restriction on the label must be upheld.

1.3.2 Crop Residues

Barley - GAP: 15–22.5 g a.i./ha, PHI 60 days.
Canada: Residue studies were conducted in Ontario, Manitoba and Alberta. Fifteen grain samples were analyzed for thifensulfuron methyl residues treated at 20–120 g a.i./ha and 70 days PHI. Resultant residues from all the samples were below the LOQ of 0.02 ppm.
US: Residue studies were conducted in Colorado, Idaho, Oregon, and North Dakota. Ten grain samples were analyzed for thifensulfuron methyl residues at rates ranging from 17.5 g a.i./ha and 97 days PHI to 140 g a.i./ha and 71 days PHI. Resultant residues from all the samples were below the sensitivity of the method (LOQ of 0.02 ppm).

Mixed grain (barley and oats) - GAP: 15–22.5 g a.i./ha, PHI 60 days.
Canada: Residue studies were conducted in Ontario. Three samples of grain were analyzed for residues of thifensulfuron methyl at application rates of 20, 40, and 80 g a.i./ha and 70 days PHI. Resultant residues in all the samples were below the sensitivity of the method (LOQ < 0.02 ppm).

Wheat - GAP: 15–22.5 g a.i./ha, PHI 60 days.
Canada: Residue studies were conducted in Alberta and Saskatchewan. Fifteen samples of grain were analyzed for residues of thifensulfuron methyl at application rates ranging from 30 g a.i./ha and 83 days PHI to 120 g a.i./ha and 99 days PHI, all samples resulted in residues below 0.02 ppm (LOQ).
US: Residue studies were conducted in Ohio, Colorado, Minnesota, North Dakota and South Dakota. Sixteen grain samples were analyzed for thifensulfuron methyl residues at rates ranging from 17.5 g a.i./ha and 97 days PHI to 280 g a.i./ha and 77 days PHI. Resultant residues from all the samples were below the LOQ of 0.02 ppm.

Oats - GAP: 15–22.5 g a.i./ha, PHI 60 days.
Canada: 12 samples (Alberta and Ontario) of oat grain treated at 20 g a.i./ha and 76 days PHI to 120 g a.i./ha and 99 days PHI; all the samples resulted in residues below the LOQ of 0.02 ppm.

Soybeans - GAP: 4.8 g a.i./ha, 60 days PHI.
Canada: 12 samples treated at 8 g a.i./ha and PHI of 109–156 days (Ontario, 1988); all the samples resulted in residues at < 0.05 ppm.
US: 16 samples treated (1986–87, 10 States) from 17.5 to 70.0 g a.i./ha and 45 to 68 days PHI; all the samples resulted in residues below LOQ of < 0.05 ppm.
Six samples (US data, 1987) treated at 17 g a.i./ha and 56 to 68 days PHI; all the samples resulted in residues below 0.05 ppm.

STS soybeans - GAP: 4.8 g a.i./ha, 60 days PHI.
Canada: 16 samples were treated (4 locations in Ontario) with Pinnacle at 37.5 g a.i./ha and 60 days PHI resulted in all samples with residues below the LOQ of < 0.05 ppm.

Tomatoes - GAP - 6 g a.i./ha and 45 days PHI.
The results from 11 supervised crop field trials in Canada at GAP were < 0.005 ppm (as per LOD of the method).

Canola and flax - GAP: 15 or 30 g a.i./ha (1-2x gap) and 62–64 days PHI.
Canada: Residue trials were conducted in Alberta (canola: 5 trials, flax: 3 trials), Saskatchewan (canola: 6 trials, flax: 4 trials) and Manitoba (canola: 4 trials, flax: 4 trials). Resulting residues in canola and flax samples were < LOQ (0.02 ppm), respectively in all the trials conducted in Alberta, Saskatchewan and Manitoba.

Promulgation of MRLs:
Tomatoes - 0.07 ppm (concentration factor for dried tomatoes of 14.3× was applied to RAC MRL of 0.005 ppm to cover MRL in RAC as well as tomato processed commodities

Canola and flax - 0.02 ppm

Crop residues conclusions
MOR have been evaluated in the residue file for barley, mixed grains (barley and oats), wheat and oats and MRL proposed was 0.02 ppm, respectively. For soybeans including STS soyabeans, the proposed MRL was 0.05 ppm. MRLs are established on tomatoes at 0.07 ppm and on flax, rapeseed (canola) at 0.02 ppm in Division 15, Table II of the FDR. Other domestic uses for which MRLs are currently not established include wheat, barley, oats and soybeans. These domestic commodities currently are covered under the general Regulations, B.15.002(1) of the FDR at ≤ 0.01 ppm. However, MRLs have been proposed at the LOQ of 0.02 ppm for domestic use on wheat, barley and oats and proposed at the LOQ of 0.05 ppm for domestic use on soybeans in the residue file and should be promulgated in Division 15, Table II of the FDR.

1.3.3 Livestock Feeding Studies - Residue Trials

The PMRA review indicated that livestock feeding studies were not previously reviewed for thifensulfuron methyl. The review stated that the petitioner submitted a waiver request for livestock feeding studies for expansion of use to canola and flax. The rationale of the waiver request was based on the fact that canola and flax seeds used as livestock feed at < LOQ (0.02 ppm at 2x gap), respectively would result in negligible residues in animal tissues. Therefore, the waiver request was granted by the PMRA. No livestock studies were reviewed as per information in the PMRA residue file.

1.3.4 Livestock feeding study - Residue Trials Conclusions

The PMRA Level C1 preliminary review for deficiencies indicated that according to RCGs (DIR98-02), a feeding restriction does not replace a feeding study. The petitioner should be advised that expansion of use to feed items should not be considered until a feeding study was conducted. A feeding study, as noted in the review would be required for any expansion of use and in order to establish MRLs on meat, milk and eggs.

1.3.5 Confined and Field Crop Rotational Studies

The PMRA previously reviewed a confined crop rotational study for thifensulfuron methyl (AMR-256-84) in rotational crops. Beets (root crop), peas (legume vegetables) and sunflowers (oil seed crop) in this study were grown to maturity in a greenhouse using loamy sand soil that had previously been treated with radiolabelled thifensulfuron methyl (thiophene-2 - ^{14}C) at 0.086 kg a.i./ha and 0.094 kg a.i./ha, respectively. Crops were planted 30 days and 120 days after treatment, respectively. Total radiolabelled thifensulfuron methyl residues were 17.9 ppb for the 30 days aged soil and 9.2 ppb for the 120 days aged soil, respectively.

Combustion analysis results in edible beet root, pea and sunflower seeds showed < 1.0 ppb –2.0 ppb and 1.0 ppb–5.0 ppb total radiolabelled thifensulfuron methyl residues in 120 days and 30 days studies, respectively. Total radiolabelled thifensulfuron methyl residues in foliage grown in the 30 days soil were below 10 ppb except for 22 ppb in mature beet foliage and 54 ppb after 43 days and 17 ppb at maturity in sunflower foliage, respectively. Foliage of crops grown in soil at 120 days after treatment showed that radiolabelled thifensulfuron methyl residues were greater than 10 ppb only in mature sunflower foliage, at 12 ppb.

Extraction and analysis results of samples with thifensulfuron methyl radiolabelled residues showed that greater than 10 ppb were extracted into acetone/water at recovery of 76–85%. HPLC analysis showed that a 43 day immature sunflower foliage sample from the 30 days soil contained 2 ppb thifensulfuron methyl radiolabelled residues; and a mature beet foliage and sunflower foliage samples each contained 1 ppb thifensulfuron methyl radiolabelled residues, respectively.

The PMRA review that radiolabelled residues did not accumulate in the rotational crops grown in loamy sand soil treated 30 and 120 days earlier with thiophene-2-^{14}C labelled thifensulfuron methyl at application rates of 0.086 and 0.094 kg a.i./ha, respectively. Radiolabelled residues in the three mature crop samples were < 5 ppb.

A minor use proposal for use expansion of thifensulfuron methyl on tomatoes concluded that thifensulfuron methyl residues were not expected in crops rotated to tomatoes at an exaggerated rate (14–16 × proposed GAP for tomatoes); and concluded that additional field rotational studies were not required as a result of the minor use proposal review.

1.3.6 Confined and field crop rotational studies conclusions

Confined crop rotational study for chicory is required; and if available should be submitted by a data call in for re-evaluation.

1.3.7 Residue Decline Studies

The review on file for residue data on mixed grains (barley/oats, whole plant, grain and straw) indicated that residues declined from 0.33 ppm at 2 days PHI to < 0.05 ppm at 28 days PHI, respectively. The tomato minor use residue results of all the residue trials reviewed showed that the thifensulfuron methyl residues in/on tomato RAC were negligible (< LOQ, LOQ= 0.02 ppm). Given that the proposed PHI was 45 days and that the pesticide was not applied when edible portion of the plant was formed, no residue decline study was required in support of the tomato minor use proposal Residue Chemistry Guidelines, RCGs, DIR98-02).

A deficiency was noted and required for a residue decline study for chicory or other tuber crops in a minor use proposal review for use of thifensulfuron methyl on chicory.

1.3.8 Residue decline study conclusion

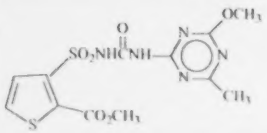
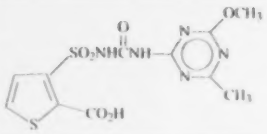
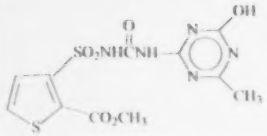
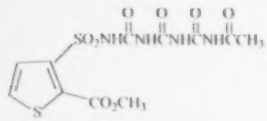
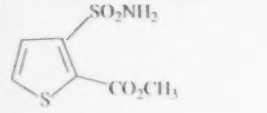
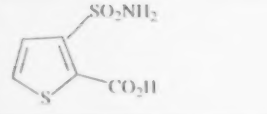
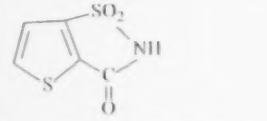
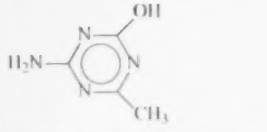
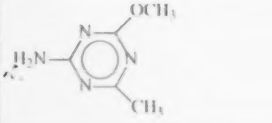
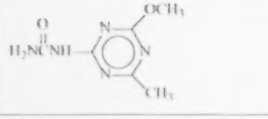
A chicory or other tuber crops residue decline study is required from the sponsor/registrant.

Appendix VIII Water Monitoring Data

A search for thifensulfuron methyl water monitoring data in Canada revealed that routine analysis for thifensulfuron methyl is not conducted. Water monitoring data for the sulfonyl-ureas that are currently under re-evaluation were requested from provincial and territorial departments responsible for water quality monitoring. In addition, requests were submitted to Environment Canada, the Department of Fisheries and Oceans and the drinking water subcommittee through Health Canada. Much of the data received from Environment Canada are preliminary, in addition, information regarding the use of thifensulfuron methyl in the vicinity of the sampling sites was not available. Thifensulfuron methyl was not detected in Alberta drinking water reservoirs, whereas, it was detected in two drinking water reservoirs in Saskatchewan and five drinking water reservoirs in Manitoba. Three dugouts that were known drinking water sources were sampled and one of these dugouts had thifensulfuron methyl detections at a detection frequency of 92%. Thifensulfuron methyl was not detected in five prairie rivers and six wetlands sampled. The concentrations of mobile pesticides in surface water are directly related to the frequency and timing of monitoring in relation to pesticide application and runoff events. Therefore, timing and frequency of sampling is likely to be the most important factor influencing the concentration detected and the frequency of detections. In view of the uncertainty caused by the above factors, the limited water monitoring data, that were available, were not used in the environmental risk assessment.

Given the scarcity of data available in Canada for residues of thifensulfuron methyl in water, US databases were searched for detections of thifensulfuron methyl. Thifensulfuron methyl was not included in the analytes that were measured in samples contained in either of these databases.

Appendix IX Major Transformation Products of Thifensulfuron Methyl

thifensulfuron methyl methyl 3-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)carbamoyl]sulfamoyl]-2-thiophenecarboxylate	
thifensulfuron acid 3-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)carbamoyl]sulfamoyl]-2-thiophenecarboxyl	
O-desmethylthifensulfuron methyl 3-[[(4-hydroxy-6-methyl-1,3,5-triazin-2-yl)carbamoyl] sulfamoyl]-2-thiophenecarboxylate	
2-ester-3-triuret methyl 3-[[(acetylamino)carbonylamino]-carbonylamino]sulphonyl]-2-thiphenecarboxylate	
2-ester-3-sulfonamide methyl 3-(aminosulphonyl)-2-thiophenecarboxylate	
2-acid-3-sulfonamide 3-(aminosulphonyl)-2-thiophenecarboxylic acid	
thiophene sulfonimide thieno[2,3-d]isothiazol-3(2H)-one, 1,1-dioxide	
triazine amine 4-methoxy-6-methyl-1,3,5-triazin-2-amine	
O-desmethyl triazine amine 4-hydroxy-6-methyl-1,3,5-triazin-2-amine	
triazine urea N-(4-methoxy-6-methyl-1,3,5-triazin-2-yl) urea	

Appendix X Environmental Fate and toxicity

Table 1 Environmental Fate of Thifensulfuron Methyl and its Transformation Products

Study type	Test material	Study Conditions	Value or Endpoint	Interpretation	Major transformation products
Abiotic transformation					
Hydrolysis	Thifensulfuron methyl	30 d	22°C 50°C pH 5 31.3 d 0.98 d pH 7 27.3 d 3.8 d pH 9 14.6 d 0.44 d	Major route of transformation under acidic and basic conditions	Not reported
			25°C 45°C pH 5 4–6 d 1.6 d pH 7 181–190 d 10.4 d pH 9 90–145 d 0.45 d	Major route of transformation under acidic conditions	2-ester-3-sulfonamide and 2-ester-3-triuret, triazine amine
		Hydrolysis kinetics @ 28°C	pH 4 1.2 d pH 5 11.5 d pH 9 4.1 d pH 10 0.25 d	Major route of transformation under acidic and basic conditions	Not reported
Phototransformation - soil	Thifensulfuron methyl	Silt loam (pH 5.4, sand 2%, silt 81%, clay 17%, OM 4.3%)	irradiated: 14–18 d dark control: 21–26 d	Not a major route of transformation	
Phototransformation - water	Thifensulfuron methyl	25°C	irradiated dark control pH 5 4.1 d 25 d pH 7 5.2 d 184 d pH 9 4.0 d 16 d	Major route of transformation	Triazine amine, triazine urea
Phototransformation - air	Thifensulfuron methyl	Indirect phototransformation	42 h	Major route of transformation	
Biotransformation					
Soil - aerobic	Thifensulfuron methyl	24–25°C; ten soils: pH 5.2–8.1; % OM 0.23–7.6	Half-life: 0.75–7 d	Non persistent	Not reported
Soil - aerobic	Thifensulfuron methyl	20°C (three soils) 25°C (two soils) Soils characteristics not reported	DT_{50} @ 25°C 2–6 d	Non persistent	
	Thifensulfuron acid		DT_{50} @ 20°C 20–157 d DT_{50} @ 25°C 2.2–365	Moderately persistent to persistent	
	O-desmethyl thifensulfuron		DT_{50} @ 20°C < 3 d DT_{50} @ 25°C 10.8–15.3 d	Non persistent to slightly persistent	
	Thiophene sulfonamide		DT_{50} @ 20°C 41–69 d DT_{50} @ 25°C 9.6–96 d	Non persistent to moderately persistent	
	Triazine amine		DT_{50} @ 20°C 22–43 d DT_{50} @ 25°C 240 d	Slightly persistent to persistent	
	2-acid-3-sulfonamide		DT_{50} @ 25°C 6–7 d	Non persistent	

Study type	Test material	Study Conditions	Value or Endpoint	Interpretation	Major transformation products
Soil - anaerobic	Thifensulfuron methyl	20°C; soil characteristics not reported	DT_{50} @ 20°C 5 d	Non persistent	Not reported
Water/sediment - aerobic	Thifensulfuron methyl	20°C; two systems, pH 8-9 (water)	Half-life 17 d (ditch, high OM sediment)	Non to slightly persistent. No significant accumulation in the sediment	Thifensulfuron acid; 2-acid-3-sulfonamide
			Half-life 14–17 d (river, low OM sediment)		Thifensulfuron acid
		20°C; 182 d, two systems, pH 6.9 and 8.5	DT_{50} 21 d (water); DT_{50} 27 d (whole system)	Slightly persistent	Thifensulfuron acid, O-desmethyl thifensulfuron methyl, O-desmethyl thifensulfuron acid, 2-acid-3-sulfonamide, triazine urea, triazine amine (all in water)
		2 systems (Netherland), not described	DT_{50} 15–16 d (whole system)	Slightly persistent	Not reported
Water/sediment - aerobic	Thifensulfuron methyl	2 systems, not described	DT_{50} 18–26 d (water) DT_{50} 60–86 d (water) DT_{50} 21–27 d (whole system) DT_{50} 71–91 d (whole system)	Moderately persistent	Thifensulfuron acid, O-desmethyl thifensulfuron acid, 2-acid-3-sulfonamide, triazine urea, triazine amine,(all in water)
	Thifensulfuron acid	Not reported	DT_{50} 66–109 d (water)	Moderately persistent	
	O-desmethyl thifensulfuron acid		DT_{50} 27–51 d (water)	Slightly persistent	
	2-acid-3-sulfonamide		DT_{50} 182 d (water)	Persistent	
	Triazine urea		DT_{50} 182 d (water)	Persistent	
	Triazine amine		DT_{50} 49–71 d (water)	Moderately persistent	
Water/sediment-anaerobic	Thifensulfuron methyl	25°C; pond water with loamy sand, pH 4.9, 3.9% OM	Half-life 28 d	Slightly persistent	2-acid-3-sulfonamide, 2-ester-3-sulfonamide
		3 systems (USA), not described	DT_{50} 18–21 d (whole system)	Slightly persistent	Thifensulfuron acid, 2-acid-3-sulfonamide, 2-acid-3-sulfonic acid, 2-ester-3-sulfonamide

Study type	Test material	Study Conditions	Value or Endpoint	Interpretation	Major transformation products
Mobility					
Adsorption/ desorption	Thifensulfuron methyl	25°C; two sandy loam (pH 6.5–6.6, 1.1–2.1% OM) and two silt loam (pH 5.2–5.4, 4.3–7.5% OM)	Sandy loam K_d 0.081–0.19 K_{OC} 13–16 Silt loam K_d 1.25–1.38 K_{OC} 29–55	High to very high mobility	2-acid-3-sulfonamide, 2-ester-3-sulfonamide, O-desmethyl thifensulfuron
Adsorption/ desorption	Thifensulfuron acid	Three soils, pH 5.7–7.7, %OC 1.2–2.6	K_{OC} 6.9–13.5	Very high mobility	
	O-desmethyl thifensulfuron		K_{OC} 34–199	High to moderate mobility	
	Thiophene sulfonamide		K_{OC} 2.6–4.3	Very high mobility	
	Triazine amine	Four soils, pH 5.3–6.3, %OC 0.46–3.02	K_{OC} 46–226	Very high to moderate mobility	
Soil column leaching	Thifensulfuron methyl (thiophene-2-^{14}C)	Four soils (pH 5.2–6.9, 0.8–7.5% OM) non-aged	% recovered in leachate as thifensulfuron methyl Loamy sand: 75% Sandy loam: 94% Silt loam: 76% Silt loam: 60%		Thifensulfuron acid (3–7%)
	Thifensulfuron methyl (thiophene-2-^{14}C and triazine-2-^{14}C)	Silt loam aged for 6 d at 25°C	% recovered in leachate as thifensulfuron methyl 35% (^{14}C-thiophene) 24% (^{14}C-triazine)		Thifensulfuron acid (29% from ^{14}C-thiophene) 26% from ^{14}C-triazine)
Field studies					
Field dissipation	Thifensulfuron methyl (thiophene-2-^{14}C and triazine-2-^{14}C)	Five Canadian sites: Saskatoon, SK Calgary, AB London, ON Kentville, NS Fisher Branch, MB	DT_{50} (thiophene-2-^{14}C): SK loamy sand 12.8 d; AB loam N/A; ON sandy loam 10.5 d; NS sandy loam 5.8 d; MB silty loam 6.0 d DT_{50} (triazine-2-^{14}C): N/A; 11.7 d; 16.5 d; 6.2 d No radioactivity found below 30 cm depth		Thifensulfuron acid, 2-acid-3-sulfonamide, 2-acid-3-sulfonic acid, 2-ester-3-sulfonamide, O-desmethyl thifensulfuron, thiophene sulfonimide

Table 2 Environmental Toxicity of Thifensulfuron Methyl and its Transformation Products

Organism	Study type	Species	Test material	Endpoint	Value (effect)	Effect of concern
Terrestrial Species						
Invertebrate	Acute oral	Honeybee (*Apis mellifera*)	Thifensulfuron methyl (98%)	48-h LD_{50}	7.1 µg a.i./bee	Mortality
	Acute contact	Earthworm (*Eisenia foetida*)	Thifensulfuron methyl (95%)	14-d LC_{50}, NOEC	>2000 mg a.i./kg soil >2000 mg a.i./kg soil	Mortality
		Honeybee (*Apis mellifera*)	Thifensulfuron methyl (98%)	48-h LD_{50}	>100 µg a.i./bee	Mortality
		Predatory mite (*Typhlodromus pyri*)	formulation: Thifensulfuron methyl 75 WG 82 g EP/ha	14-d beneficial capacity	4.6% R=1.24	Mortality Reproduction
		Parasitic wasp (*Aphidius rhopalosiphi*)		48-h beneficial capacity	-11% R=1.3	Mortality Fecundity
		Green lacewing (*Chrysoperla carnea*)		14-d beneficial capacity	3.6% R=1.2	Mortality Reproduction
		Carabid beetle (*Poecilus cupreus*)	formulation: Thifensulfuron methyl 75 WG 10 g EP/ha	14-d beneficial capacity	3.3% R=0.69	Mortality Food consumption
		Staphylinid beetle (*Aleochara bilineata*)		beneficial capacity	0% 0% 35% 6%	Mortality Food consumption Oviposition Hatching rate
Birds	Acute oral	Bobwhite quail (*Colinus virginianus*)	Thifensulfuron methyl (98%)	LD_{50}	1524 mg a.i./kg bw	Mortality
		Mallard duck (*Anas platyrhynchos*)		LD_{50}	>2510 mg a.i./kg bw	Mortality
	Dietary	Bobwhite quail (*Colinus virginianus*)		LC_{50}	>5620 mg a.i./kg diet	Mortality
	Dietary	Mallard duck (*Anas platyrhynchos*)		LC_{50}	5620 mg a.i./kg diet	Mortality
	Reproduction	Bobwhite quail (*Colinus virginianus*)		NOEC	250 mg a.i./kg diet	Reproduction
		Mallard duck (*Anas platyrhynchos*)		NOEC	1250 mg a.i./kg diet	Reproduction

Organism	Study type	Species	Test material	Endpoint	Value (effect)	Effect of concern
Mammals	Acute oral	Rat	Thifensulfuron methyl (96.5%)	LD_{50}	>5000 mg a.i./kg bw	Mortality
		Rabbit	Thifensulfuron methyl (97%)	LD_{50}	>2600 mg a.i./kg bw	Mortality
	Dietary	Rat	Thifensulfuron methyl (93.6-95.6%)	90 d NOEC	100 mg a.i./kg diet	Growth
		Mouse	Thifensulfuron methyl (95-98%)	90 d NOEC	7500 mg a.i./kg diet	Growth
		Dog	Thifensulfuron methyl (95.6%)	90 d NOEC	1500 mg a.i./kg diet	Growth
		Rat	Thifensulfuron methyl (95.6 -98%)	2-yr NOEC	500 mg a.i./kg diet ♂ 25 mg a.i./kg diet ♀	Development
		Dog	Thifensulfuron methyl (98.2-94.8%)	1-yr NOEC	7500 mg a.i./kg diet (♂ and ♀)	Development
	Reproduc-tion	Rat	Thifensulfuron methyl (93.6-95.6%)	NOEC (1-generation)	7500 mg a.i./kg diet	Reproduction
		Rat	Thifensulfuron methyl (95.6-98%)	NOEC (2-generation)	2500 mg a.i./kg diet	Reproduction
Plants	Seedling emergence	10 plant species	Thifensulfuron methyl (rate 35 g a.i./ha)	EC_{25} NOEL	0.1–6.1 g a.i./ha >2.2–>17.5 g a.i./ha	Height emergence
	Vegetative vigour			EC_{25}	0.03–52 g a.i./ha	
Freshwater Organisms						
Invertebrate	Acute	*Daphnia magna*	Thifensulfuron methyl	48-h EC_{50}	>1000 mg a.i./L	Immobility
					470 mg a.i./L	
					>970 mg a.i./L	
			Thifensulfuron acid		>0.8 mg a.i./L	
Invertebrate	Acute	*Daphnia magna*	2-acid-3-sulfonamid		>1.2 mg a.i./L	
			O-desmethyl thifensulfuron		>1.1 mg a.i./L	
			Triazine urea		>1.3 mg a.i./L	
	Chronic		Thifensulfuron methyl	21-d NOEC	100 mg a.i./L	
			Triazine urea		>97 mg a.i./L	

Organism	Study type	Species	Test material	Endpoint	Value (effect)	Effect of concern
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	Thifensulfuron methyl (98%)	96-h LC_{50}	>100 mg a.i./L	Mortality
			Thifensulfuron acid	96-h LC_{50}	>1 mg a.i./L	Mortality
			2-acid-3-sulfonamid		>1.1 mg a.i./L	
			O-desmethyl thifensulfuron		>0.94 mg a.i./L	
			Triazine urea		>1 mg a.i./L	
		Bluegill sunfish (*Lepomis macrochirus*)	Thifensulfuron methyl (98%)	96-h LC_{50}	>100 mg a.i./L	Mortality
		Channel catfish (*Ictalurus punctatus*)			360 mg a.i./L	
	Chronic (Early Life Stage)	Rainbow trout (*Oncorhynchus mykiss*)	Thifensulfuron methyl (98%)	NOEC	250 mg a.i./L	
Algae	Acute	Green alga (*Selenastrum capricornutum*)	Thifensulfuron methyl (99%)	EC_{50}, NOEC	>15.7 µg a.i./L, 15.7 µg a.i./L	Growth and reproduction
				EC_{50}	15.9 µg a.i./L	
			Thifensulfuron acid	EC_{50}	1020 µg a.i./L	
			2-acid-3-sulfonamid		1300 µg a.i./L	
			O-desmethyl thifensulfuron		1280 µg a.i./L	
			Triazine urea		11 000 µg a.i./L	
		Blue-green algae (*Anabaena flos-aquae*)	Thifensulfuron methyl (99%)	EC_{50}, NOEC	>26.3 µg a.i./L, 26.3 µg a.i./L	Growth and reproduction
		Diatom (*Navicula pelliculosa*)		EC_{50}, NOEC	>8.15 µg a.i./L, 8.15 µg a.i./L	
Vascular Plants	Acute	Duck weed (*Lemna gibba*)	Thifensulfuron methyl	14-d EC_{50}, NOEC	1.3 µg a.i./L, 0.5 µg a.i./L	
				14-d EC_{50}, NOEC	1.6 µg a.i./L, 0.5 µg a.i./L	Biomass and frond counts
				14-d EC_{50}, NOEC	1.72 µg a.i./L, 0.5 µg a.i./L	Frond counts and biomass
				14-d EC_{50}, NOEC	1.3 µg a.i./L, 0.5 µg a.i./L	Frond counts
			Thifensulfuron acid	14-d EC_{50}	>1000 µg a.i./L	
			2-acid-3-sulfonamid		>1000 µg a.i./L	
			O-desmethyl thifensulfuron		>1000 µg a.i./L	
			Triazine urea		>10 000 µg a.i./L	

Organism	Study type	Species	Test material	Endpoint	Value (effect)	Effect of concern
Marine/Estuarine organisms						
Algae	Acute	*Skeletonema costatum*	Thifensulfuron methyl	EC_{50} NOEC	>17.5 µg a.i./L 17.5 µg a.i./L	

Table 3 Summary of Screening Level Risk Assessment of Thifensulfuron Methyl to Terrestrial Organisms

Organism	Exposure	Endpoint reported	Use Rate (g a.i./ha)	EEC	RQ[1]
Invertebrates					
Earthworm	Acute	NOEC = 200 mg a.i./kg soil	3.3	1.5×10^{-3} mg a.i./kg soil	3.5×10^{-5}
			15	7.0×10^{-3} mg a.i./kg soil	7.5×10^{-4}
Honeybee	Acute contact	NOEC = 0.71 µg a.i./bee (0.795 kg a.i./ha)	3.3	3.3×10^{-3} kg a.i./ha	4.1×10^{-3}
			15	1.5×10^{-2} kg a.i./ha	2.0×10^{-2}
Birds					
Mallard	Dietary	NOEC = 5620 mg a.i./kg diet	3.3	0.11 mg a.i./kg diet	7.5×10^{-5}
			15	0.51 mg a.i./kg diet	9.7×10^{-5}
	Reproduction	NOEC = 250 mg a.i./kg diet	3.3	0.11 mg a.i./kg diet	3.4×10^{-4}
			15	0.51 mg a.i./kg diet	4.1×10^{-4}
Bobwhite quail	Dietary	NOEC = 562 mg a.i./kg diet	3.3	0.58 mg a.i./kg diet	1.0×10^{-3}
			15	2.63 mg a.i./kg diet	4.7×10^{-3}
	Reproduction	NOEC = 250 mg a.i./kg diet	3.3	0.58 mg a.i./kg diet	2.3×10^{-3}
			15	2.63 mg a.i./kg diet	1.05×10^{-2}
Mammals					
Rat	Dietary	NOAEL = 100 mg a.i./kg diet	3.3	1.66 mg a.i./kg diet	1.7×10^{-2}
			15	7.57 mg a.i./kg diet	7.6×10^{-2}
	Reproduction	NOAEL = 2500 mg a.i./kg diet	3.3	1.66 mg a.i./kg diet	6.6×10^{-4}
			15	7.57 mg a.i./kg diet	3.0×10^{-3}
Plants					
Plants	Seedling emergence (sugar beet)	EC_{25} = 0.1 g a.i./ha	3.3	3.3 g a.i./ha	**33**
			15	15 g a.i./ha	**110**
	Vegetative vigour (sugar beet)	EC_{25} = 0.03 g a.i./ha	3.3	3.3 g a.i./ha	**150**
			15	15 g a.i./ha	**500**

[1] **Bold fonts indicates exceedance of LOC**

Table 4 Refined Risk Assessment of Thifensulfuron Methyl to Terrestrial Plants

Organism	Exposure	EC25	Use Rate (g a.i./ha)	% application rate to reach EC25	Drift EEC*	RQ[1]
Plants	Seedling emergence (sugar beet)	0.1 g a.i./ha	3.3	3	0.2 g a.i./ha	**2**
			15	0.7	0.9 g a.i./ha	**7**
	Vegetative vigour (sugar beet)	0.03 g a.i./ha	3.3	0.9	0.2 g a.i./ha	**9**
			15	0.2	0.9 g a.i./ha	**30**
* Based on drift of 6% for a default droplet size of medium (herbicides).						

[1] **Bold fonts indicates exceedance of LOC**

Table 5 Summary of Screening Level Risk Assessment of Thifensulfuron Methyl to Aquatic Organisms

Organism	Exposure	Species	Endpoint reported (mg a.i./L)	Endpoint for RA* (mg a.i./L)	Use Rate (g a.i./ha)	EEC** (mg a.i./L)	RQ[1]
Freshwater Species							
Invertebrate	Acute	*D. magna*	LC_{50} = 470	235	3.3	4.0×10^{-4}	1.7×10^{-6}
					15	1.9×10^{-3}	8.1×10^{-6}
	Chronic	*D. magna*	NOEC = 100	100	3.3	4.0×10^{-4}	4.0×10^{-6}
					15	1.9×10^{-3}	1.9×10^{-5}
Fish	Acute	Rainbow trout	LC_{50}>100	10	3.3	4.0×10^{-4}	4.0×10^{-5}
					15	1.9×10^{-3}	1.9×10^{-4}
	Chronic	Rainbow trout (Early Life Cycle)	NOEC = 250	250	3.3	4.0×10^{-4}	1.6×10^{-6}
					15	1.9×10^{-3}	7.5×10^{-6}
Plant	Acute	Diatom	NOEC = 0.00815	0.00815	3.3	4.0×10^{-4}	4.9×10^{-2}
					15	1.9×10^{-3}	0.2
	Acute	Duckweed	NOEC = 0.0005	0.0005	3.3	4.0×10^{-4}	0.8
					15	1.9×10^{-3}	**3.75**
Amphibian	Acute	Rainbow trout (surrogate)	LC_{50}>100	10	3.3	2.2×10^{-5}	2.2×10^{-6}
					15	1.0×10^{-4}	1.0×10^{-5}
	Chronic	Fish (Early Life Cycle) (surrogate)	NOEC = 250	250	3.3	2.2×10^{-5}	8.8×10^{-8}
					15	1.0×10^{-4}	4.0×10^{-7}

Organism	Exposure	Species	Endpoint reported (mg a.i./L)	Endpoint for RA* (mg a.i./L)	Use Rate (g a.i./ha)	EEC** (mg a.i./L)	RQ[1]
Estuarine and Marine Species							
Plant	Acute	Algae	NOEC = 0.0175	0.0175	3.3	4.0×10^{-4}	2.3×10^{-2}
					15	1.9×10^{-3}	0.11

* Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.
** EEC based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic organisms.

[1] **Bold fonts indicates exceedance of LOC**

Table 6 Summary of Screening Level Risk Assessment of Thifensulfuron Methyl Transformation Products to Aquatic Organisms

Organism	Exposure	Species	Endpoint reported (mg a.i./L)	Endpoint for RA* (mg a.i./L)	Use Rate (g a.i./ha)	EEC** (mg a.i./L)	RQ
Thifensulfuron acid							
Invertebrate	Acute	*D. magna*	LC_{50} >0.8	0.4	3.3	4.0×10^{-4}	1.0×10^{-4}
					15	1.9×10^{-3}	8.1×10^{-6}
Fish	Acute	Rainbow trout	LC_{50}>1	0.1	3.3	4.0×10^{-4}	4.0×10^{-3}
					15	1.9×10^{-3}	1.9×10^{-2}
Algae	Acute	Green alga	EC_{50}~1020	510	3.3	4.0×10^{-4}	7.8×10^{-7}
					15	1.9×10^{-3}	3.7×10^{-6}
Plants	Acute	Duckweed	EC_{50}>1000	500	3.3	4.0×10^{-4}	8.0×10^{-7}
					15	1.9×10^{-3}	3.8×10^{-6}
Amphibian	Acute	Rainbow trout (surogate)	LC_{50}>1	0.1	3.3	2.2×10^{-3}	2.2×10^{-2}
					15	1.0×10^{-2}	1.0×10^{-1}
2-acid-3-sulfonamid							
Invertebrate	Acute	*D. magna*	LC_{50}>1.2	0.6	3.3	4.0×10^{-4}	6.7×10^{-4}
					15	1.9×10^{-3}	3.2×10^{-3}
Fish	Acute	Rainbow trout	LC_{50}>1.1	0.1	3.3	4.0×10^{-4}	4.0×10^{-3}
					15	1.9×10^{-3}	1.9×10^{-2}
Algae	Acute	Green alga	EC_{50}~1300	650	3.3	4.0×10^{-4}	6.15×10^{-7}
					15	1.9×10^{-3}	2.9×10^{-6}
Plants	Acute	Duckweed	EC_{50}>1000	500	3.3	4.0×10^{-4}	8.0×10^{-7}
					15	1.9×10^{-3}	3.8×10^{-6}

Organism	Exposure	Species	Endpoint reported (mg a.i./L)	Endpoint for RA* (mg a.i./L)	Use Rate (g a.i./ha)	EEC** (mg a.i./L)	RQ
Amphibian	Acute	Rainbow trout (surogate)	LC_{50}>1.1	0.1	3.3	2.2×10^{-3}	2.2×10^{-2}
					15	1.0×10^{-2}	1.0×10^{-1}
O-desmethyl thifensulfuron							
Invertebrate	Acute	*D. magna*	LC_{50}>1.1	0.1	3.3	4.0×10^{-4}	4.0×10^{-3}
					15	1.9×10^{-3}	1.9×10^{-2}
Fish	Acute	Rainbow trout	LC_{50}>0.94	0.09	3.3	4.0×10^{-4}	4.4×10^{-3}
					15	1.9×10^{-3}	2.1×10^{-2}
Algae	Acute	Green alga	EC_{50} - 1280	640	3.3	4.0×10^{-4}	6.25×10^{-7}
					15	1.9×10^{-3}	3.0×10^{-6}
Plants	Acute	Duckweed	EC_{50}>1000	500	3.3	4.0×10^{-4}	8.0×10^{-7}
					15	1.9×10^{-3}	3.8×10^{-6}
Amphibian	Acute	Rainbow trout (surogate)	LC_{50}>0.94	0.09	3.3	2.2×10^{-3}	2.0×10^{-2}
					15	1.0×10^{-2}	1.1×10^{-1}
Triazine urea							
Invertebrate	Acute	*D. magna*	LC_{50} > 1.3	0.65	3.3	4.0×10^{-4}	6.15×10^{-4}
					15	1.9×10^{-3}	2.9×10^{-3}
	Chronic		NOEC > 97	97	3.3	4.0×10^{-4}	4.1×10^{-6}
					15	1.9×10^{-3}	1.95×10^{-5}
Fish	Acute	Rainbow trout	LC_{50}>1	0.5	3.3	4.0×10^{-4}	8.0×10^{-4}
					15	1.9×10^{-3}	3.8×10^{-3}
Algae	Acute	Green alga	EC_{50}>11 000	5500	3.3	4.0×10^{-4}	7.2×10^{-8}
					15	1.9×10^{-3}	3.45×10^{-7}
Plants	Acute	Duckweed	EC_{50}>10 000	5000	3.3	4.0×10^{-4}	8.0×10^{-8}
					15	1.9×10^{-3}	3.8×10^{-7}
Amphibian	Acute	Rainbow trout (surogate)	LC_{50}>1	0.1	3.3	2.2×10^{-3}	2.2×10^{-2}
					15	1.0×10^{-2}	1.0×10^{-1}

* Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.
** Assumption that the EECs for transformation products are the same as those for the parent compound rimsulfuron

Table 7 Refined Risk Assessment of Thifensulfuron Methyl to Aquatic Organisms from Spray Drift

Organism	Exposure	EC25 (mg a.i./L)	Use Rate (g a.i./ha)	Drift EEC* (mg a.i./L)	RQ
Plants	Acute	0.0005	3.3	0.000025	5×10^{-2}
			15	0.0001	0.2
* Based on drift of 6% for a default droplet size of medium (herbicides).					

Table 8 Risk Assesment of Thifensulfuron Methyl for Freshwater Organisms from Predicted Runoff

Toxicity endpoint	EEC (µg a.i./L)*	Endpoint (µg a.i./L)	RQ[1]
Invertebrates			
Acute	0.76	47 000	2×10^{-5}
Chronic	0.67	100 000	7×10^{-6}
Fish			
Acute	0.76	10 000	8×10^{-5}
Chronic	0.67	250 000	3×10^{-6}
Algae			
Acute	0.76	8.15	9×10^{-2}
Vascular plants			
Acute	0.76	0.5	**1.52**
* 90th percentile of peak and 21d runoff values for acute for chronic, respectively			

[1] **Bold fonts indicates exceedance of LOC**

Appendix XI Label Amendments for Commercial Class Products Containing Thifensulfuron methyl

Canadian commercial end-use product labels must be amended to include the following statements to further protect workers and the environment.

FOR ALL FORMULATIONS:

Add to **DIRECTIONS FOR USE:**

- Do not re-enter treated fields until 12 hours after application.
- Apply only when the potential for drift to areas of human habitation or areas of human activity (houses, cottages, schools and recreational areas) is minimal. Take into consideration wind speed, wind direction, temperature, application equipment and sprayer settings.

Field sprayer application:

- **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty.
- **DO NOT** apply with spray droplets smaller than the ASAE medium classification.
- **DO NOT** apply by air.

Buffer zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer, inter-row hooded sprayer, spot treatment, soil drench, and soil incorporation.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, pastures, rangelands, and shrublands), sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of application	Buffer zone (metres) required for the protection of:		
	Terrestrial habitat	Aquatic habitats of water depths:	
		< 1 m	> 1 m
Field sprayer*	25	1	0

* For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy, the labelled buffer zone can be reduced by 30%.

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

Add to **ENVIRONMENTAL HAZARDS:**

- **TOXIC** to plants. Observe buffer zones specified under DIRECTIONS FOR USE.
- To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to: heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g. soils that are compacted or fine textured such as clay).
- Avoid application of this product when heavy rain is forecast.
- Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

Add to **PRECAUTIONS:**

- Wear long-sleeved shirt, long pants, socks, and chemical-resistant gloves and footwear during mixing, loading, application, clean-up and repair. Chemical-resistant gloves are not required while operating groundboom sprayers.

FOR WETTABLE GRANULE/SOLUBLE GRANULE FORMULATIONS:

Add to **DIRECTIONS FOR USE:**

- Thifensulfuron methyl is formulated as a wettable granule or a soluble granule sealed within a water-soluble package (WSP). Drop intact WSP directly into spray tank. The WSP and pesticide will dissolve readily in water.
- Do not allow the WSP to become wet prior to use. Do not handle individual WSP with wet hands or wet gloves as this may cause breakage. Do not remove WSP from over-wrap container except for immediate use.
- Do not open WSP or attempt to remove the contents from them. The contents are not designed to be re-measured or subdivided.
- Do not use opened or punctured WSP.
- If broken WSP is found when the over-wrap bag is opened, avoid contact with, and inhalation of the product. Handle with chemical-resistant gloves and dispose of broken WSP according to the DISPOSAL section.

FOR FORMULATION PCP Reg. No. 22575:
On the secondary panel of the supplemental label for fall application on winter wheat, the text which reads "FALL APPLICATION ON WINTER WHEAT IN EASTERN CANADA" on page 6 must be revised to read "FALL APPLICATION ON WINTER WHEAT IN ONTARIO ONLY" to correct the inconsistent regional use restrictions.

FOR FORMULATION PCP Reg. No. 22352 and 22575:

The leaf stage for wild buckwheat which reads "cotyledon 1–3 leaf stage" must be revised to read either "the cotyledon - 3 leaf stage" or "the 1–3 leaf stage" whichever is correct.